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MERCURIAL INUNCTIONS IN THE TREATMENT OF SYPHILIS

EXCRETION OF MERCURY FOLLOWING USE OF MILD MERCUROUS CHLORIDE INUNCTIONS; MODE OF ABSORPTION OF MERCURY FROM SKIN

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Mercurial inunctions have been used from the earliest days in the treatment of syphilis. They are efficient and secure an adequate excretion of mercury when they are properly performed. Nevertheless, they have the objection of being uncleanly, of occasionally leading to irritation of the skin, and likewise of leading to disclosure of the condition. Therefore, if another more cleanly and yet equally efficient preparation of mercury could be found, it would be most valuable.

As long ago as 1905, Neisser and Siebert [1] suggested such a preparation entitled, "Kalomel Salve," or "Unguentum Heyden." It consisted of a colloidal mild mercurous chloride made of 75 per cent mild mercurous chloride and 25 per cent albumin, with a mercury content of 66 per cent. The dose to be inuncted was 10 Gm. They reported that usually after the fifth day mercury was found in the urine. In experiments on animals they found in microscopic studies that particles of mild mercurous chloride were present only in the openings of the hair follicles, while with the official

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1. Neisser and Siebert: Med. Klin. **1**:9, 1904.

unguentum cinereum (unguentum hydrargyri, U. S. P.) the mercury particles were found deep in the follicles—the latter observation corresponding to the previous findings of Fürbringer and Neumann.[2] The clinical results obtained by Neisser and Siebert were not satisfactory, and they added 2 per cent finely divided metallic mercury, using 6 Gm. a day as a dose. Even with this preparation their results were not especially satisfactory, though prompter effects were noted.

In 1912, Matzenauer [3] mentioned the use of another proprietary mild mercurous chloride preparation, "Calomel Ebaga." This ointment was reported to have as a base a combination of alkali with stearic and palmitic acid, mineral oil and a little fat. One ointment contained 30 per cent mercury and the other, "Ebaga Mercuriale," 15 per cent mercury. Matzenauer claimed, as advantages, freedom from the necessity to employ vigorous friction, absence of irritation and rapid disappearance from the skin. Buchtala [4] studied two patients who used the 15 per cent ointment in 6 Gm. doses for fourteen and eleven days, respectively, and one patient who used the 30 per cent salve in 3 Gm. doses for seven days. The results compared well with those of Bürgi and Lomholt, using the official ointment. However, his studies were not carried out over a sufficiently long time to permit definite conclusions.

In 1917, Wile and Elliott [5] also made absorption experiments with mild mercurous chloride ointment and with some other mercurial ointments. Their method of detecting mercury was such that they reported that they could find 0.025 mg. in 300 cc. of solution. They did not make quantitative estimations of mercury, so that the results could not be very accurate. They found that mercury salicylate inunctions were not easily absorbed. Of the oxides of mercury, the red oxide seemed to be absorbed more rapidly than the yellow oxide ointment. They found the oleate of mercury to be absorbed only as rapidly as the mercury salicylate. They concluded that the mode of absorption of mercury salicylate is both by volatilization and by direct absorption; that nonvolatile salts are absorbed through the skin, but that elimination and absorption are far slower than in the case of salts having a high vapor pressure; that the more rapid appearance of mercury in the urine, in the case of the volatile salts, is probably due to the combined action of volatilization and inhalation through the lungs and absorption through the skin; that in

2. Fürbringer and Neumann, quoted by Binz: Lectures on Pharmacology, translated by Peter Latham, London, The New Sydenham Society, 1897, vol. 2, p. 133.

3. Matzenauer, R.: Wien. med. Wchnschr. **44**:2882, 1912.

4. Buchtala: Ztschr. f. physiol. Chem. **83**:272, 1913.

5. Wile, U. J., and Elliott, J. A.: Mode of Absorption of Mercury in the Inunction Treatment of Syphilis, J. A. M. A. **68**:1024 (April 7) 1917.

the order of rapidity of absorption, the metallic mercury ointment ranks over mild mercurous chloride, though the latter is appreciably absorbed through volatilization, and that volatile salts should be used instead of nonvolatile salts, even though not so cleanly. They suggested that further studies should be made to see if mild mercurous chloride may not be used in preference, as it is cleaner.

The following year, Schamberg, Kolmer, Raiziss and Gavron[6] likewise tried out the efficiency of mild mercurous chloride ointment. They were particularly desirous of finding out the way in which mercury is absorbed from the skin, and, secondly, whether mild mercurous chloride ointment is as well absorbed as unguentum hydrargyri. They used a mixture of mild mercurous chloride, 3 Gm., hydrous wool fat, 1 Gm., and benzoinated lard, 2 Gm., making a 50 per cent preparation. Two rabbits were placed in a partitioned box. One had his head entirely outside of the inclosed box, thus breathing uncontaminated air. The other rabbit, through an aperture in the partition, had his head in the compartment containing the inuncted body of the first rabbit, and yet not touching him, the theory being that if he did get any mercury in his system, he would have to respire it from rabbit 1 by way of volatilization, inasmuch as the mercurial application was made only on the body of rabbit 1. Nothing was said in their paper, however, about how the rabbits were fed; and it may be suspected that rabbit 2 could easily have got some mercury from his food, which would presumably have come in contact with the inuncted mercury on the body of rabbit 1. In their experiments, two rabbits were treated with unguentum hydrargyri and three with the mild mercurous chloride ointment. The various tests were simply to show the presence of mercury and were not quantitative. The conclusions were that the chief method of absorption was by the skin; that rabbits may absorb some mercury by breathing, but that respiratory absorption is far the less important; that metallic mercury ointment is more volatile than mild mercurous chloride ointment of the same strength; that mild mercurous chloride ointment is fully as well absorbed as diluted mercurial ointment, U. S. P. "Indeed, we have the impression that calomel is absorbed with greater facility"; that there is no reason why mild mercurous chloride ointment should not supplant the unclean diluted mercurial ointment, U. S. P., which has been so long in use.

Clinically, the formula of Schamberg et al. was tried out in 1919 by Cole and Littman[7] on fifty-four patients. They found it to be

6. Schamberg, J. F.; Kolmer, J. A.; Raiziss, G. W., and Gavron, J. L.: Experimental Studies of the Mode of Adsorption of Mercury When Applied by Inunction, J. A. M. A. **70**:142 (Jan. 19) 1918.

7. Cole, H. N., and Littman, Sidney: A Clinical Study on the Use of Calomel Inunctions, J. A. M. A. **73**:1409 (Nov. 8) 1919.

totally inefficient against primary and secondary syphilis. The inunctions, though carefully performed, rarely produced salivation or gingivitis. They occasionally produced dermatitis. These findings naturally were disappointing, as even today a cleanly mercurial inunction would not be out of place.

Despite these clinical findings, the modern textbooks still express a difference of opinion as to the value of mild mercurous chloride inunctions. Thus Darier and Pollitzer [8] advise: "A 30 per cent calomel ointment seems to be not less efficient and has the advantage of cleanliness." Ormsby [9] mentions the mild mercurous chloride ointment and the claims of efficiency made by Schamberg et al. and then states that Cole and Littman found it inferior. Hazen [10] mentions the formula of the mild mercurous chloride rubs of Schamberg. Sutton,[11] in the latest edition of his textbook, simply mentions mild mercurous chloride inunctions, and reports that they have been found to be inferior. Pusey [12] advises against their use. Andrews [13] uses unguentum hydrargyri only. Lomholt,[14] in his new volume on therapy in syphilis, writes as follows: "Aside from metallic mercury, other mercury combinations, for instance, mild mercurous chloride, have also been used for inunctions, although with only slight success" (*wenn auch durchweg mit recht mittelmässigen Resultaten*). This variance of opinion seemed to us to call for further investigation of the mercury excretion after mild mercurous chloride inunctions.

EXPERIMENTAL PROCEDURE

Six male patients were selected in the Cleveland City Hospital; two were white and four were colored; none had any eruption of the skin. Four grams of 50 per cent mild mercurous chloride ointment (mild mercurous chloride, 3 Gm., hydrous wool fat, 1 Gm., and benzoinated lard, 2 Gm.) was rubbed into the skin daily for thirty days, except with one patient who salivated with the fourteenth rub. The inunctions were

8. Darier, J.: A Textbook of Dermatology, edited by S. Pollitzer, Philadelphia, Lea & Febiger, 1920, p. 633.

9. Ormsby, O. S.: A Practical Treatise on Diseases of the Skin for the Use of Students and Practitioners, ed. 2, Philadelphia, Lea & Febiger, 1921, p. 764.

10. Hazen, H. H.: Syphilis: A Treatise on Etiology, Pathology, Diagnosis, Prognosis, Prophylaxis and Treatment, St. Louis, C. V. Mosby Company, 1919, p. 580.

11. Sutton, R. L.: Diseases of the Skin, ed. 8, St. Louis, C. V. Mosby Company, 1931, p. 952.

12. Pusey, W. A.: Principles and Practice of Dermatology, New York, D. Appleton & Company, 1929, p. 685.

13. Andrews, G. C.: Diseases of the Skin, Philadelphia, W. B. Saunders Company, 1930, p. 748.

14. Lomholt, S.: Syphilis Therapie, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1918, vol. 18, p. 49.

for thirty minutes each time, and were done carefully under the eyes of an observer. Twenty-four hour urine and fecal specimens were collected three days each week, followed by an intermission of four days. The three daily specimens were combined for analysis. In a two day period beforehand, urine and feces were analyzed to establish the absence of mercury, and three twenty-four hour specimens were also collected one week after the course of treatments was completed.

EXPERIMENTAL RESULTS

The individual charts of the patients, with the daily urinary and fecal mercury excretions, are shown in chart 1, the urinary above, the fecal below, the base line. The curves of the median urinary and fecal mercury excretions, which were determined from the numerical data on the individual patients, are represented by the dotted lines. The curve of the median urinary mercury excretion shows a very slow, progressive rise, reaching a maximum of 0.09 mg. of mercury per day at the end of the four weeks of treatment. The curve of the median fecal mercury excretion shows a rapid initial increase to 0.45 mg. of mercury per day at the end of the first week, remains almost constant during the second and third weeks, and then declines but slightly to the end of the fourth week (0.37 mg. of mercury per day). There was only one case of salivation (W. A. Y.); the patient became salivated at the fourteenth rub, when urinary mercury excretion was 0.03 mg. of mercury a day. An early salivation at such a low level, we believe, is due to a special "predisposition."

The numerical data on the individual patients have been combined and reduced to medians and extremes. These numerical ranges showing the urinary, fecal and total mercury excretion at the end of each week, for four weeks, are presented in the table.

COMPARISON OF RESULTS

The value of the 50 per cent mild mercurous chloride ointment can be judged best by comparing the curve of the median urinary excretion with that when 50 per cent U. S. P. metallic mercury ointment was used and with that when 5 per cent metallic mercury ointment was used, as published in a previous paper.[15] The urinary mercury appears to reflect the actively circulating mercury better than does the fecal or the total mercury, and is therefore used as the index of efficiency. The simple inunctions with 50 per cent metallic mercury and 5 per cent metallic mercury were also administered by daily rubs of 4 Gm. of the ointment over a period of four weeks, making a total of 14 Gm. of mercury in

15. Cole, H. N.; Schreiber, N., and Sollmann, T.: Mercurial Ointments in Treatment of Syphilis: Their Absorption as Measured by Studies on Excretion, Arch. Dermat. & Syph. **21**:372 (March) 1930.

the case of the former, and 1.3 Gm. in the case of the latter. A comparison of the medians of the urinary, fecal and total mercury excretion for these three ointments is shown in the table and in chart 2.

It may be seen that the urinary excretion of mercury with the 50 per cent mild mercurous chloride ointment is much less than that with the 50 per cent metallic mercury ointment, but it coincides practically with that of the 5 per cent metallic mercury ointment. In other words, the absorption of mild mercurous chloride, as judged by the urinary excretion of mercury, is only about one-eighth that of the 50 per cent metallic

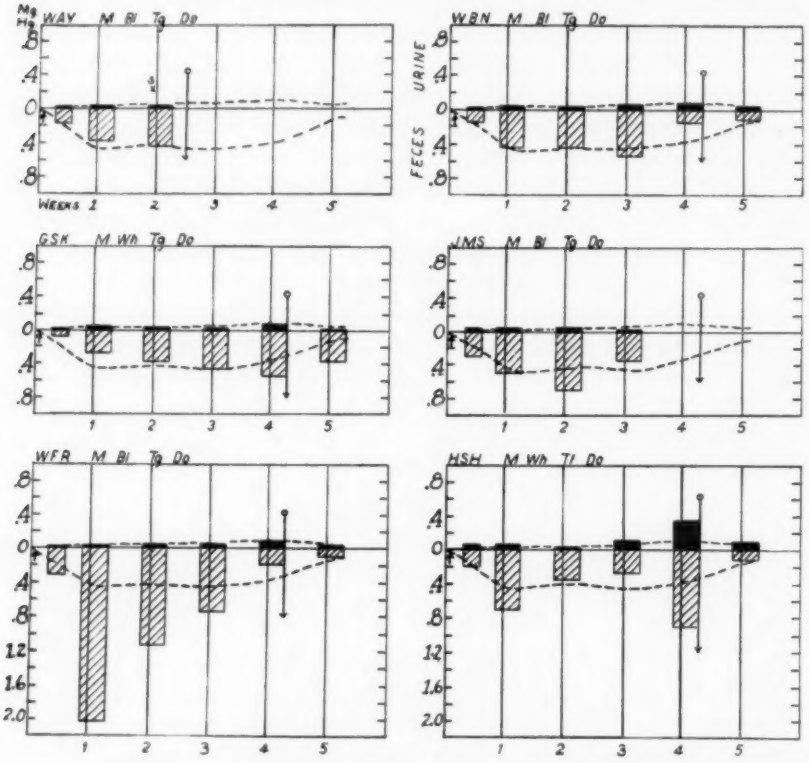

Chart 1.—Individual charts of patients who had received simple daily inunctions with 50 per cent mild mercurous chloride ointment. The solid blocks above the zero line represent the urinary excretion of mercury; the hatched blocks inverted below the line, the fecal excretion of mercury. The broken lines show the median excretion for all patients. The horizontal lines correspond to milligrams of mercury per day, each division representing 0.2 mg.; the vertical lines, to the duration of the administration, in weeks. The short ascending arrows indicate the beginning, the long descending arrows, the end of the treatment. *S* indicates the onset of salivation. The letters above each chart identify the patient, the sex (*M* or *F*), the race (*Wh* or *B*), the condition of the teeth (*T*, teeth; *ex*, excellent; *g*, good; *f*, fair; *p*, poor), and the cutaneous lesions (*D*, *fol*, *mac*, *pap*.).

Comparison of Medians and Extremes of Daily Excretion of Mercury

Mercurial Preparation Used	Excretion Studied	Mg. of Mercury Excreted per Day at the End of						Cumulative Mercury Excretion at End of 28 Days, Mg. Hg
		Three, Four Days	First Week	Second Week	Third Week	Fourth Week	One Week After Conclusion of Treatment	
50% mild mercurous chloride	Urine	0.03 (0.01-0.06)	0.04 (0.01-0.07)	0.04 (0.03-0.05)	0.05 (0.02-0.11)	0.09 (0.07-0.35)	0.05 (0.02-0.10)	1.3
	Feces	0.19 (0.06-0.31)	0.45 (0.28-2.02)	0.43 (0.34-1.13)	0.45 (0.23-0.75)	0.37 (0.15-0.91)	0.11 (0.07-0.39)	10.7
	Total	0.23 (0.09-0.36)	0.50 (0.32-2.04)	0.47 (0.43-1.17)	0.47 (0.34-0.80)	0.45 (0.22-1.26)	0.19 (0.11-0.41)	12.0
5% mercury ointment (4.6% Hg)	Urine	0.02 (0.02-0.06)	0.05 (0.03-0.08)	0.07 (0.06-0.16)	0.11 (0.06-0.15)	0.15 (0.12-0.20)	0.09 (0.04-0.13)	2.1
	Feces	0.10 (0.04-0.27)	0.16 (0.05-0.30)	0.17 (0.06-0.34)	0.28 (0.05-0.39)	0.25 (0.32-0.42)	0.17 (0.07-0.36)	5.3
	Total	0.12 (0.56-0.31)	0.22 (0.09-0.33)	0.31 (0.12-0.44)	0.39 (0.18-0.49)	0.38 (0.32-0.59)	0.27 (0.11-0.49)	7.4
50% mercury ointment (U.S.P.), simple inunction	Urine	.....	0.12 (0.02-0.40)	0.33 (0.15-0.70)	0.58 (0.31-1.77)	0.83 (0.38-3.0)	0.73 (0.65-1.30)	10.7
	Feces	.....	0.35 (0.02-0.72)	0.48 (0.30-1.25)	0.44 (0.18-0.91)	0.45 (0.18-1.30)	0.45 (0.37-0.78)	13.5
	Total	.....	0.56 (0.18-1.02)	0.94 (0.52-1.45)	1.06 (0.49-2.68)	1.44 (0.78-3.52)	1.18 (1.02-1.76)	24.2

mercury ointment. On the other hand, the fecal excretion of mercury is almost the same as that with the 50 per cent metallic mercury ointment. Since there is no reason to assume that the mercury circulates in a different form when it is applied as mild mercurous chloride than when it is administered as metallic mercury, it appears probable that this discrepancy is due to extraneous causes. In this connection, it may be recalled that it has been suggested by Cole, Schreiber and Sollmann [15] that the fecal excretion with inunctions is probably largely mercury that has been swallowed because of contact with the hands. This would presumably be similar for metallic mercury and mild mercurous chloride inunctions. If so, it represents chiefly unabsorbed mercury and therefore would have no therapeutic significance.

The low urinary excretion of mild mercurous chloride definitely establishes that it is absorbed much less readily than metallic mercury.

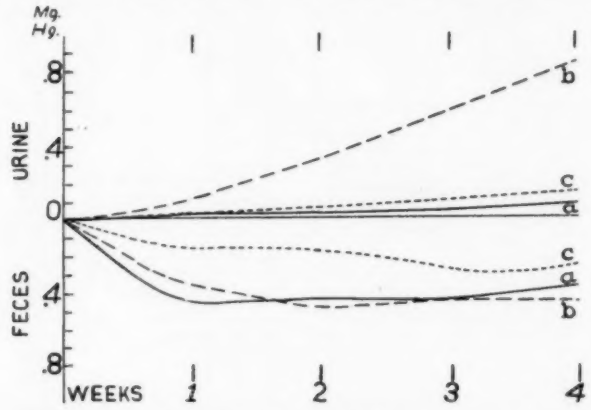

Chart 2.—Comparison of the medians of the daily excretion of mercury after simple inunctions with 50 per cent mild mercurous chloride ointment (*a*); 50 per cent metallic mercury ointment, U. S. P. (*b*), and 5 per cent metallic mercury ointment (*c*).

This could be explained by the lower volatility of the mild mercurous chloride, by its failure to penetrate the follicles or by its greater resistance to the chemical changes leading to its solution. The last is not probable, especially in view of the absorbability of intramuscular injections of mild mercurous chloride. The first explanation, lesser volatility, would imply that at least five sixths of the metallic mercury is absorbed as vapor through the lungs. Although we are not prepared to deny that a part of the mercury may be absorbed in this manner, there is reason to doubt that this channel is of major importance in therapeutic inunction. Binz [16] concluded that the absorption takes place

16. Binz: Lectures on Pharmacology, translated by Peter Latham, London, The New Sydenham Society, 1897, vol. 2, p. 133.

from the parts rubbed, for he detected the mercury in the body when its entrance to the respiratory organs had been completely prevented. Jenkins [17] was skeptical of the absorption of mercury through volatilization in the process of inunction. For example, he placed a dish of metallic mercury in an incubator at body heat for forty-eight hours. The loss from volatilization was 0.0001 Gm. Two small globules of mercury in a beaker in an incubator at body temperature for five days appeared to be just the same size at the end of this time. He further took four patients, plugged their nostrils and had them breathe through a tube leading to the outside air. They were inuncted for twenty minutes with 2 Gm. of unguentum hydrargyri. They were then sent out into the yard, and in the evening their clothes were changed and they were washed. Patient 1, a psoriatic person, was salivated in nine days; patient 2, whose blood gave a positive Wassermann reaction, had sore gums from the eighth to the thirteenth day, and with a dose of 2 drachms (3.5 Gm.) he was salivated two days later; patient 3, with syphilitic ulcer of the throat, was healed in ten days; patient 4, with syphilitic hemiplegia, was better in four days, and the facial paralysis was gone on the fourteenth day. The results in the syphilitic patients were almost as good as after administration of arsphenamine, and yet there had been very little opportunity for absorption by way of the lungs. The strongly toxic effects of the inhalation of heated mercury do not invalidate these conclusions, since the experiments of Cole, Gericke and Sollmann [18] and others indicate that much of the so-called inhalation of mercury in mercury inhalations is simply mercury vapor deposited on the mucous membranes of the nose, mouth and throat, and then swallowed.

The key to the explanation of the limited absorption of mild mercurous chloride is probably furnished by the studies of Fürbringer and Neumann,[2] who found that the globules of mercury, on being rubbed into the skin, pass into the hair follicles as far even as the hair bulb. They also pass into the sebaceous follicles. The orifices of the sweat ducts frequently contain some of the globules, but they are rarely seen in a sweat canal and never in a sweat gland. The globules in the hair follicles are absorbed from these parts, for in a few days they are coated with oxide and diminish in number, and in a few weeks they disappear entirely, while in the internal organs mercury is present chemically but not in globules. This work of Fürbringer and Neumann has also been confirmed by Zwick.[19] It was this theory that led Cole, Gericke and

17. Jenkins, C. E.: Brit. J. Dermat. **33**:135, 1921.

18. Cole, H. N.; Gericke, A. J., and Sollmann, T.: Clean Inunction Treatment of Syphilis with Mercury, J. A. M. A. **77**:2022 (Dec. 24) 1921.

19. Zwick, K. G.: A Microscopic Study of Mercury Absorption from the Skin, J. A. M. A. **83**:1821 (Dec. 6) 1924.

Sollmann [20] to advocate the clean inunctions; namely, that the mercury absorbed is the mercury rubbed into the hair follicles and sebaceous glands. On the other hand, Neisser and Siebert [1] reported that in their experiments on animals particles of mild mercurous chloride were found only in the openings of the hair follicles, in contrast to metallic mercury, which was found in a deeper location. This difference between the distribution of mercury and mild mercurous chloride in the cutaneous structures is probably due to their physical state: the pliability of the drops of liquid mercury permits them to be massaged into the ducts, while the rigid mild mercurous chloride is only smeared over the surface, just as metallic mercury can be pressed through a chamois skin which would retain the finest mild mercurous chloride. In accordance with this, we have found [21] that the absorption of colloidal mercury inunctions is relatively poor, notwithstanding the fine comminution; for the colloidal metals behave as rigid solids. Lomholt [14] stated that Eschbaum and Aufrecht had noted this low mercury excretion after colloidal mercury inunctions.

SUMMARY

1. Because of inconclusive clinical results with 50 per cent mild mercurous chloride inunctions, it was thought best to obtain a better criterion of its true absorption from the skin through a study of the mercury excretions.

2. To six adult male patients, a series of from eighteen to thirty rubs, with a median of thirty rubs, was administered. There was one salivation at fourteen days, probably an idiosyncrasy.

3. At the end of four weeks there was a median mercury excretion of but 0.09 mg. and a median fecal excretion of 0.37 mg. The relatively high fecal excretion is probably to be explained as absorption from the fingers by way of the mouth.

4. This low mercury excretion after 50 per cent mild mercurous chloride inunctions may be best compared to that which occurs with 5 per cent metallic mercury inunctions, with which there was a median urinary excretion of 0.15 mg. at the end of four weeks and a median fecal excretion of 0.25 mg. at the end of four weeks.

5. The explanation for the low urinary mercury excretion after 50 per cent mild mercurous chloride inunctions probably lies in the difficulty of rubbing the hard particles of mild mercurous chloride into the hair follicles. Consequently, it is poorly absorbed.

1352 Hanna Building.

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20. Cole, H. N.; Gericke, A. J., and Sollmann, T.: Treatment of Syphilis by Mercury Inhalations, Arch. Dermat. & Syph. **5**:18 (Jan.) 1922.

21. Cole, H. N.; Schreiber, N., and Sollmann, T.: To be published.

ABSTRACT OF DISCUSSION

DR. WILLIAM H. GUY, Pittsburgh: We are again indebted to Dr. Cole and his co-workers for a painstaking piece of work with reference to the therapeutics of mercury by inunction in the treatment of syphilis. The fact that this is a negative finding only increases the value of the work. Many men have been led astray by the clean type of administration of mild mercurous chloride. A graph indicating the relative absorption and elimination of the drugs which parallel each other indicates that the amount of mercury which is absorbed when it is administered in the form of mild mercurous chloride is almost nil. Any therapeutic effect that is obtained must be interpreted by the presence of mercury in the urine.

I think, to summarize Dr. Cole's paper briefly, one could say that mercury in the form of mild mercurous chloride by inunction is just about as useful as a crutch at a fireman's ball.

DR. J. P. THORNLEY, New York: I should like to ask one question, and that is, whether the elimination of the mild mercurous chloride by the feces may or may not have been due to excretion in the bile. Has any effort been made to determine that? Evidently the mercury has got into the patient either by the mouth or by the skin and has been excreted by the feces. Is it not possible that the source of some of this is from the bile? Mild mercurous chloride has been believed to have an effect on the bile and the liver for ages, the pharmacologist to the contrary notwithstanding.

DR. ROBERT C. JAMIESON, Detroit: I feel that Dr. Cole has given us a valuable contribution on the inunction method of treating syphilis even though, as Dr. Guy said, it is of negative quality. We have all had some feeling about this, and up to the present I have never had any definite indication as to whether mild mercurous chloride was or was not of definite value. I feel that one way in which Dr. Cole has helped us is in giving us a very definite answer for some of the detail men who have been trying to sell us high-priced preparations of mild mercurous chloride for inunction purposes.

DR. HAROLD N. COLE, Cleveland: In answer to Dr. Thornley, I believe that he will find, if he looks up his pharmacology, that mild mercurous chloride has been a favored agent of the laity for treating conditions in the liver for a long time, but the pharmacologist does not agree with this. It has been found not to have any effect on the liver itself. If mild mercurous chloride were excreted by way of the bile, it would indicate that there was a high mercury content in the blood stream, and this would be indicated by the urinary excretion, and this is what it does not show. If we give protiodides by mouth, there will also be a high fecal excretion, but we have to depend on the urinary excretion of mercury to measure the height of the mercury that is present in the blood stream.

EPIDERMOMYCOSIS AT THE UNIVERSITY OF CALIFORNIA

STUDY III

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AND
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BERKELEY, CALIF.
AND
H. J. TEMPLETON, M.D.
OAKLAND, CALIF.

In 1928 a committee of three, Drs. Robert Legge, Lee Bonar and H. J. Templeton, was appointed to consider the problem of epidermomycosis at the University of California. In August, 1928, the feet of 3,105 freshman matriculants were examined [1] at the beginning and at the end of the fall gymnasium work by the same medical examiners. Fifty-one and five-tenths per cent of the men showed clinical evidence of ringworm of the feet, as did 15.3 per cent of the women.

As all freshmen are required to take work in the gymnasium, the committee had an excellent opportunity to study the effect of exposure to gymnasium environment on the incidence of ringworm of the feet. Beginning the semester with an involvement of 51.5 per cent, as stated, 1,000 of the men at the end of the semester had an involvement of 78.6 per cent, *an increase of 27 per cent.* During the same period of time the incidence among 997 women students increased only 2 per cent.[2] Although there is a possibility of error in these figures because of some changes in the personnel of the students studied, they are in the main correct. The committee believed that this enormous difference in the increase among the male students as compared to that among the women could be largely explained by the hygiene of the two gymnasiums. The

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From the Cowell Memorial Hospital and the Department of Botany, University of California.

Read at the Fifty-Fifth Annual Meeting of the American Dermatological Association, Havana, Cuba, May, 1932.

1. Legge, Robert T.; Bonar, Lee, and Templeton, H. J.: Ringworm of the Feet, J. A. M. A. **92**:1507 (May 4) 1929.

2. Legge, Robert T.; Bonar, Lee, and Templeton, H. J.: Incidence of Foot Ringworm Among College Students: Its Relation to Gymnasium Hygiene, J. A. M. A. **93**:170 (July 20) 1929.

women worked in a new, well lighted, airy building with tile or cement floors, while the men's building was old, poorly lighted and ventilated and supplied with wooden floors and runways. Even more important was the fact that the women were never permitted to put the bare feet on the floor, being forced to wear rubber sandals, while the men commonly walked barefoot on the damp wooden floors.

OCCURRENCE OF DERMATOPHYTES AS SAPROPHYTES

One of the group, Dr. Bonar, studied the occurrence of the various fungi as saprophytes on gymnasium floors and runways and in swimming pools, boxing gloves and other gymnasium equipment. He also investigated the possibility of growing Trichophyton interdigitale on sterile cotton, silk, wool, horn, sound wood, rotted wood, algal slime-covered wood, rubber and leather. Next, he studied the effect of the commonly used dry-cleaning processes and laundering on clothing infected with

TABLE 1.—*Dermatophytes Found in Ringworm of the Feet*

Year	Number of Patients	Number of Plants	Number of Patients Giving Positive Results	Type of Dermatophyte Recovered			
				Trichophyton Interdigitale	Trichophyton Rosaceum	E. Cruris	Unidentified
1929.....	221	2,932	110	45	21	41	3
1930.....	209	3,762	71	47	7	15	2
1931.....	205	3,690	65	14	24	21	6
Total.....	635	10,384	246	106	52	77	11

Trichophyton interdigitale. Lastly, he investigated the possibility of wood flooring acquiring and retaining any fungistatic properties after having been impregnated with various chemicals. All these studies, which have such a direct and practical bearing on the control of ringworm in gymnasiums, have been reported by Dr. Bonar elsewhere.[2a].

OCCURRENCE OF DERMATOPHYTES AS PATHOGENS

In order to learn what species of dermatophytes were to be found in the ringworm infections of our students, a study was made covering three separate years. All three surveys were made during the late summer and early fall months, when ringworm of the feet is at the peak of its incidence and severity in this district. All the cases were of ringworm of the feet, and in nearly all instances the scrapings were taken from lesions between the toes.

2a. Bonar, Lee, and Dreyer, Alice D.: Studies on Ringworm Funguses with Reference to Certain Public Health Problems, Am. J. Pub. Health **22**:909 (Sept.) 1932.

TECHNIC OF CULTURE

As mediums for the isolation work Sabouraud's dextrose peptone agar and a modification of that used by Leonian were used. The latter has been made up as follows:

	Gm.
Dihydrogen potassium phosphate	1.2
Magnesium sulphate	0.5
Dextrose	6.0
Malt extract (desiccated)	6.0
Agar	20.0
Distilled water	1,000.0
Initial p_H	about 5.4

This medium, when cleared with white of egg, gives a good clear agar, which is essential for the isolation work. The fungi grow readily on this medium, but bacterial growth is less rapid than on the Sabouraud's medium with its rich content of peptone and sugar and more alkaline reaction. The concentration of food materials in Sabouraud's medium is far greater than is necessary for a vigorous development of the fungi, and this excess of materials stimulates an excessive degree of vegetation, with a much lower percentage of spore production than is obtained in the medium of lower concentration. This is a condition that can be demonstrated with many fungi, and since one is desirous in most cases of securing the best degree of sporulation possible, it is an advantage to employ the medium that will most nearly yield the desired results. Cultures grown on this more dilute medium are much more satisfactory for studies of the morphology of the fungus, since there are more abundant reproduction and less matting of the mycelia into an unmanageable turf over the surface of the medium. Cultures on the less rich medium do not become pleomorphic as quickly as on the medium of Sabouraud. This is an advantage in the laboratory where a series of studies are being made and where it is desired to maintain a single cultural strain in a reproductive condition for as long a time as possible. Duplicate cultures on Sabouraud's medium can always be used to get the typical picture of the growth on that medium at the same time. The inoculated Petri plates were kept at room temperature.

TABLE 2.—*Influence of Varying Numbers of Plants on Percentage of Positive Results*

Number of Skin Plants per Case	Number of Cases	Percentage of Positive Results
10 to 11	34	32
12 to 13	72	44
14 to 15	41	47
16, 17 or 18	43	66

Besides giving accurate information relative to the types of fungi, this work emphasized the necessity of making multiple plants of the scales from each patient onto the culture medium, a very important point in clinical and laboratory technic.

Thus, when ten or eleven plants were made on Petri dishes in the examination of each one of thirty-four patients, positive results came to 32 per cent. But when from sixteen to eighteen plants were made for

each patient in a series of forty-three patients, positive results increased to 66 per cent. In other words, when the number of plants was increased by approximately one-half, the percentage of positive results was more than doubled.

Table 2 adequately illustrates the fallacy of planting a small number of scales from a suspected case and accepting negative results as conclusive.

STUDIES OF THE FUNGICIDAL PROPERTIES OF CERTAIN CHEMICALS

Inspired by the work of Schamberg and Kolmer and their associates,[3] Kingery and Adkisson[4] and Osborne and Hitchcock,[5] the committee

TABLE 3.—*Comparative Resistance of Three Species of Fungi* *

Concentration (Aqueous)	Corrosive Mercuric Chloride			Phenol			Thymol			Benzoic Acid			Salicylic Acid			Hexylresorcinol			Pine Oil Soap Solution		
	T. interdigitale	T. rosaceum	E. cruris	T. interdigitale	T. rosaceum	E. cruris	T. interdigitale	T. rosaceum	E. cruris	T. interdigitale	T. rosaceum	E. cruris	T. interdigitale	T. rosaceum	E. cruris	T. interdigitale	T. rosaceum	E. cruris	T. interdigitale	T. rosaceum	E. cruris
Full	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	—	—	—
1:200	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	+	+
1:1,000	—	—	—	+	+	+	+	—	—	+	+	—	—	—	—	—	—	—	+	+	+
1:2,000	—	—	—	+	+	+	+	+	+	+	+	+	—	—	—	—	—	—	..	..	..
1:3,000	—	—	—	+	+	+	+	+	+	+	+	+	+	—	—	—	—	—	..	..	..
1:4,000	—	—	—	+	+	+	+	+	+	+	+	+	+	—	—	+	—	—	..	..	..
1:5,000	—	—	—	+	+	+	+	+	+	+	+	+	+	—	—	+	—	—	..	..	..
Control 1†	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Control 2‡	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

* Time of exposure, five minutes at 22 C.; incubation for twenty-one days at 25 C.

† Control 1: Dextrose peptone broth to which 2 loopfuls of lowest dilution of germicide was added before direct inoculation from the spore suspension. It was believed that this would approximate the amount of germicide that would be carried over when inoculations were made from the dilutions tested.

‡ Control 2: Spore suspension inoculated directly into dextrose peptone broth.

studied the fungicidal properties of a number of chemicals already in use, or proposed for use, in the treatment of ringworm of the feet. These studies necessarily duplicated some of the work of these investigators, but chemicals and remedies not mentioned by them have also

3. Schamberg, J. F., and Kolmer, J. A.: Studies in the Chemotherapy of Fungus Infections, Arch. Dermat. & Syph. **6**:746 (Dec.) 1922. Schamberg, J. F.; Brown, H., and Harkins, M. J.: The Chemotherapy of Ringworm Infection, Arch. Dermat. & Syph. **24**:1033 (Dec.) 1931.

4. Kingery, L. B., and Adkisson, A.: Certain Volatile Oils and Stearoptens as Fungicides, Arch. Dermat. & Syph. **17**:499 (April) 1928.

5. Osborne, Earl D., and Hitchcock, Blanche S.: Prophylaxis of Ringworm of the Feet, J. A. M. A. **97**:453 (Aug. 15) 1931.

been investigated. An attempt was made to demonstrate their fungicidal properties (*A*) on spore suspensions and (*B*) on infected human skin scales.

A. Fungicidal Properties of Chemicals in Vitro.—The action of the fungicide tested may be influenced by several factors, most important of which are: (1) the type of organism used, (2) the concentration of the organism in the test, (3) the concentration of the fungicide, (4) the temperature at which the test is made and (5) the time during which the fungicide acts on the organism.

In order that dependable comparable results would be attained, these variable factors were carefully controlled and reduced to a minimum.

The organism used in the greater number of tests was Trichophyton interdigitale in pure, bacteria-free cultures from thirty-five to forty days old.

In table 3 are shown comparative results on three species of dermatophytes, Trichophyton interdigitale Priestley, Trichophyton rosaceum Sabouraud and Epidermophyton cruris Castellani. Of these, Trichophyton interdigitale was shown to be consistently more resistant to the action of thymol, salicylic acid and hexylresorcinol than either of the other species, and further tests were made on this one species alone.

These results do not agree with those of some other workers [8] who have recorded Trichophyton rosaceum as more resistant than Trichophyton interdigitale, but repeated tests and checking of the results gave consistently uniform results.

The technic of fungicidal tests in vitro is as follows:

Spore suspensions were made by pouring from 5 to 10 cc. of sterile distilled water on a tube culture and washing off the spores from the culture. This was then shaken with glass beads in a shaking machine for from one-half to one hour, transferred to graduated centrifuge tubes and centrifugated at high speed for one hour. The supernatant fluid was poured off and the sediment of spores made up to a 3 per cent suspension. The fungicide was made up to the desired concentration, and to 5 cc. of this 0.1 cc. of the prepared spore suspension was added. This insured a uniform concentration of the spores in a given amount of the disinfectant.

The time allowed was five minutes, after which two loopfuls of the material were transferred to tubes containing 10 cc. of dextrose peptone broth (1 per cent dextrose and 1 per cent peptone). Slight amounts of the disinfectant would be carried over into the broth tubes with the spores, and in order to balance this, two loopfuls of the disinfectant were added to the control tubes in which the untreated spores were planted.

The experiments were carried on at from 20 to 22 C. The test cultures were incubated at 25 C. The results recorded were either complete killing or growth.

The inoculation of the treated spores into agar tubes, cooled to 40 C., and the subsequent pouring of these into plates will give better opportunity for the determination of the degree of the killing action when such action is not complete. The percentage of killing, determined by colony counts from such plates, is not entirely dependable. It is not possible to be certain that a colony appearing on the plates is a growth from a single spore rather than from a cluster of spores.

Study of Fungicides: By the use of this standardized method the number of variables in the experiment was reduced to one, that of the concentration of the fungicides under study. By a consideration of the results thus obtained, a ready comparison of the fungicidal action of different compounds or preparations can be made.

Many of the compounds shown in table 4 have been studied by previous investigators. Our results are in close accord with these earlier findings. Brief comment might be made in regard to certain of the compounds.

Sodium thiosulphate was found to be ineffective in 10 per cent solution, even when acting up to periods of forty-eight hours. This is of interest when one considers its being advocated for use in foot baths.

TABLE 4.—*Fungicidal Action on Spore Suspensions of Trichophyton Interdigitale* *

Compound	Full	1:2	1:10	1:100	1:200	1:500	1:1,000	1:2,000	1:3,000	1:4,000	1:5,000	1:10,000	1:50,000	1:100,000	Control 1	Control 2
Corrosive mercuric chloride	..	..	..	..	..	..	—	—	—	—	—	..	..	..	+	+
Phenol	..	..	..	+	..	+	+	+	+	+	+	..	..	..	+	+
Thymol	..	..	..	..	..	..	+	+	+	+	+	..	..	..	+	+
Benzoic acid	..	..	..	..	..	..	+	+	+	+	+	..	..	..	+	+
Salicylic acid	..	..	..	..	..	..	—	+	+	+	+	..	..	..	+	+
Sodium thiosulphate	..	..	+	+	..	+	+	..	..	..	..	..	..	..	+	+
Hexylresorcinol	..	..	..	..	..	..	—	..	—	+	+	..	..	..	+	+
Iodine in potassium iodide solution	..	..	..	..	..	..	..	..	..	..	..	—	—	—	+	+
Absorbine Jr.	—	+	+	+	..	..	+	..	..	..	..	..	..	..	+	+
Kerosene	+	..	..	..	..	..	..	..	..	..	..	..	..	..	+	+
Sodium hypochlorite †	—	..	..	—	..	..	+	..	..	..	+	..	..	..	+	+
Metaphen	..	..	..	..	..	+	+	+	+	+	+	..	..	..	+	+
Pine oil soap solution ‡	—	..	..	..	+	..	..	..	..	..	..	..	..	..	+	+
Merthiolate	..	..	..	..	..	..	—	—	—	—	—	..	..	+	+	+
Solution of chlorinated soda	..	..	..	—	..	—	—	..	..	..	—	..	..	..	+	+

* Exposure for five minutes at 22 C.; incubation for twenty-one days at 25 C.
† Stock solution, 4.5 per cent.
‡ Commercial preparation.

Metaphen failed to sterilize the spore suspension when used in the usual strengths of from 1 : 500 to 1 : 5,000 for the five minute period.

Kerosene in full strength showed no destruction of fungi. This has bearing on the dry cleaning of infected clothing.

Hexylresorcinol was effective in a 1 : 3,000 dilution.

Sodium hypochlorite and solution of chlorinated soda killed all of the spores in the five minute period when used in that strength (1 per cent) which has been advocated for use in foot baths. Chlorox was effective in a 1 : 5,000 dilution.

Merthiolate destroyed all spores in five minutes in all dilutions up to and including 1 : 10,000. A 1 : 100,000 dilution failed to kill.

Iodine in the form of the compound solution was effective in a 1 : 100,000 dilution. This is in accord with Schamberg's findings.

Of the various fungicides studied in vitro, the most promising were iodine and merthiolate. Chlorox and sodium hypochlorite were effective in the strengths recommended for foot baths.

Effect of Short Wave Ultraviolet Irradiation ("Cold Quartz Light") on Cultures of Trichophyton Interdigitale: Because of claims made in regard to the sterilizing properties of the new "cold quartz light" with its shorter wavelength of about 2,500 angstroms, the following experiment was undertaken:

Spore suspensions were made up in water in the center of a sterile Petri dish. The water was allowed to evaporate. The spores so spread on the glass were exposed by removing the lid of the Petri dish and irradiating at a distance of 5 inches (12.7 cm.). After irradiation the spores were worked up in a few drops of sterile water, and then agar that had been cooled to below 45 C. was poured in and subsequent growth observed.

From table 5 it is apparent that the short wave ultraviolet rays (of about 2,500 angstroms) possess definite fungicidal powers in spite of the fact that they did not completely sterilize the cultures.

TABLE 5.—*Effect of Short Wave Ultraviolet Rays on Spores of Trichophyton Interdigitale*

Irradiation	Sixth Day	Fourteenth day
None (control)	Heavy growth	Heavy growth
1 minute	Very slight growth	5 colonies
3 minutes	No growth	1 colony
6 minutes	Slight growth	13 colonies
10 minutes	No growth	No growth
15 minutes	1 colony	1 colony

B. Fungicidal Properties of Chemicals on Infected Human Skin Scales.—Studies by a number of investigators have shown that a rather large number of compounds are highly fungicidal to ringworm fungi when applied to spore suspensions of the fungi. Many of these compounds, however, have been shown to be of little or no value in everyday therapy.

Preliminary tests on spore suspensions are important for the determination of the most promising fungicides, and the elimination of those giving less promise; but high toxicity to spores in a suspension does not insure that the preparation will be of value when applied to the infected skin.

A method of determining fungicidal activity that the committee felt would give more dependable information as to the probable therapeutic value of a given compound when applied to a skin bearing the fungus infection was developed. The fungicidal action of the compound under study is tested on human skin scales in which fungi have been demonstrated by culture.

The method is as follows:

1. Skin scales from the suspected case are proved to be positive by laboratory culture, by planting numerous fragments and by determining the percentage of growth from these plants.

2. The remainder of the skin material from this same patient is cut into small fragments, about 1 mm. square.

3. These fragments are immersed in a solution of the fungicide of the desired concentration, for a definite period of time.

4. They are then removed aseptically, with forceps flamed from alcohol, to a bath of the proper solvent for removing the fungicide from the surface of the fragments.

5. The fragments are then planted in agar plates and the percentage of growth noted and compared with that in the controls.

By employing different periods of time and different concentrations of the disinfectant, an accurate measure of the action of any given compound can be worked out. The most obvious difficulty in the use of this method is that of securing sufficient material from any one patient for the making of such a series of tests. Our experience (table 2) has led us to the opinion that a minimum of twenty plants should be made for the controls in such a series and a like number for each of the intervals of time and concentrations employed. One can, however, occasionally find a patient from whom sufficient material can be collected at one time or accumulated by successive collections over a period of two or three weeks.

One factor that must be carefully determined in such a procedure is the possible action of the solvent employed. Many of the compounds to be tested are insoluble in water. In such instances other solvents must be employed and their action, if any, on the fungi within the skin scales must be tested by the routine treatment already outlined.

The larger the number of the plants employed in such work, the more dependable will be the results obtained and the lower the probable error due to irregular sampling of particulate material such as the skin scales. Because of the great amount of work involved, we have been able to test only twelve agents by this method. The results attained by this method are shown in table 6.

Alcohol (a 50 per cent solution) completely sterilized infected scales only after they had been immersed in it for one and one-half hours. This length of time would seem to preclude its practical use as a therapeutic agent. But its positive action, although slow, serves to confuse the findings in tests of other fungicides in which alcohol has been used as a diluent, except in cases when the time of exposure was so low as to preclude the possibility of alcohol having destroyed the test organisms.

Acetone exhibited no fungicidal properties on skin scales. A practical point, then, is that acetone may be used as a solvent in preparing fungicides for testing.

The same holds true in regard to carbon tetrachloride, naphtha and kerosene. They exhibited no fungicidal activity. This is also of interest in relation to the dry-cleaning processes, as one of us (Dr. Bonar) has pointed out.

Thymol in two different dilutions killed all fungi in skin scales in thirty minutes. This would seem to indicate that it has potential value as a therapeutic agent.

TABLE 6.—*Fungicidal Tests on Human Skin Scales Infected with Trichophyton Interdigitale*

Substance	Concentration	Control		10 Min.		15 Min.		20 Min.		25 Min.		30 Min.		60 Min.		90 Min.		120 Min.	
		Plants	Growth	Plants	Growth	Plants	Growth	Plants	Growth	Plants	Growth	Plants	Growth	Plants	Growth	Plants	Growth	Plants	Growth
Alcohol	50%	22	8	..	..	..	..	17	6	..	..	..	..	19	5	14	0	..	..
Acetone	100%	18	6	..	..	45	10	..	..	..	..	50	10	..	..	..	..	..	..
Carbon tetrachloride	100%	20	7	..	..	..	..	..	..	..	..	20	6	20	4	..	..	..	..
Naphtha	100%	20	7	..	..	..	..	..	..	..	..	20	3	20	4	..	..	20	4
Kerosene	100%	30	12	..	..	..	..	..	..	..	..	..	..	..	..	20	8	..	..
Thymol	3% in 50% alcohol	17	6	12	3	..	..	..	..	..	..	20	0	21	0	..	..	..	..
Thymol	5% in 95% alcohol	23	9	12	5	12	1	13	1	14	1	21	0	..	..	..	..	..	..
Benzoic acid	5% in 95% alcohol	20	7	..	..	20	6	..	..	..	..	20	0	..	..	..	..	..	..
Salicylic acid	6% in 70% alcohol	20	7	..	..	20	0	..	..	..	..	20	1	..	..	..	..	..	..
Crystol	6% in water	12	4	..	..	14	4	..	..	..	..	12	0	..	..	..	..	..	..
Absorbine Jr.	Full strength	12	5	..	..	9	3	..	..	..	..	8	3	..	..	..	..	..	..
Iodine	1:100 in water : iodine, compound solution	20	11	..	..	20	0	..	..	..	..	20	0	20	0	..	..	..	..
Iodine	1:1,000 in water : iodine, compound solution	20	11	..	..	20	0	..	..	..	..	20	0	20	0	..	..	..	..
Iodine	1:10,000 in water : iodine, compound solution	20	11	..	..	20	6	..	..	..	..	20	6	20	0	..	..	..	..
Solution of chlorinated soda*	1% in water	30	16	60	10	..	..	..	..	..	..	60	7	60	0	..	..	..	..

* The skin scales used in testing solution of chlorinated soda contained E. cruris instead of T. interdigitale.

Salicylic acid and benzoic acid were actively fungicidal in from fifteen to thirty minutes, thus justifying their empiric use in ointments for many years.

A new dye, crystol,[6] sterilized all of the scales in thirty minutes. But our work with it is open to criticism because of the fact that we could not wash all the dye off of the scales when they were removed from the solution prior to planting.

Absorbine Jr. proved to be valueless. Scales immersed in the full strength solution for thirty minutes showed no inhibition of growth of fungi.

6. Resorcin crystal violet hydrochloride: $C_{28}H_{30}N_3Cl.2C_6H_4(OH)_2$.

Solution of chlorinated soda (1 per cent) sterilized the scales in one hour.

Iodine, in the compound solution, showed the most interesting results. A 1 per cent solution (measured in terms of iodine content) sterilized all the scales in fifteen minutes. A 1:1,000 solution also sterilized all the scales in fifteen minutes. A 1:10,000 dilution sterilized all the scales in one hour. As all these dilutions are such as can be safely used on the skin, iodine would seem to be of great promise, as judged by our studies.

COMMENT

In studies of any fungicidal agent its action was first tested on spore suspensions. If the agent showed promise of value in vitro, the next logical step was to determine its activity by testing it on infected skin scales. The last step in deciding the practical value of promising agents was to try them on patients. Because of abundant clinical material it has been possible to test twenty-six agents or compounds on groups of students. Groups of from 10 to 50 students have been placed on each remedy and observed at weekly intervals. At each visit their progress was recorded, and frequent cultures of the lesions were made during the course of treatment. An attempt was then made to correlate the clinical improvement with the decreasing number of positive cultures. This work will be reported in detail later.

CONCLUSION

The occurrence of epidermomycosis among the students of the University of California has been studied. The types of the causative fungi have been determined and their life as saprophytes and pathogens studied. The fungicidal properties of many antiseptics have been tested on spore suspensions. A new method of determining the value of fungicides as judged by their action on infected skin scales has been reported.

DISCUSSION

DR. FRED D. WEIDMAN, Philadelphia: This kind of work is always in order as long as the problem of the treatment and etiology of dermatophytosis is with us, and I dare say the matter of treatment is now the outstanding problem of all. We have just embarked on a similar study at the University of Pennsylvania, including both men and women. It was found that a lesser percentage of cultures was obtained from the women than from the men, yet gymnasium conditions were just the reverse of the ones in Dr. Templeton's work. Thus, our women use an old gymnasium that was formerly occupied by the men, while the men have a new, modern one. I still feel that there must be something in the sex and in susceptibility of the patient rather than in the wood of the gymnasia to explain the lesser incidence in women.

I was a little surprised that Trichophyton rosaceum was so common on the Pacific Coast. As I recall it, only 4 or 5 cases had been described among dermatophytoses in the entire literature. Trichophyton rubrum and versicolor also yield pink cultures.

Finally, one must consider the value of students as test patients. I thought that we had ideal conditions in our university group. As at the University of California, we were dealing with a high grade, intelligent class of subjects obliged to attend the gymnasium and appear before us, but results did not work out at all ideally. The students would not do as they were told, but showed a high degree of "sales resistance." Contemporaneously with our project, another dermatologist was connected with a state penitentiary where the inmates were eager to do anything that was different from daily routine. Very shortly Dr. Howles will publish his findings comparing the various therapeutic agents tested under ideal conditions such as are a sine qua non for truly scientific results.

Dr. Howard Fox, New York: I was most interested in these findings, and was impressed by the enormous number of students whom they were able to examine. Dr. Muskatblit in our clinic recently examined the toes of a much smaller number, 100 students and also 112 patients at the dispensary for comparison. In 89 per cent of all cases there were clinical changes which suggested the possibility, at least, of a fungus infection. It was interesting to note the higher percentage of infection in students than in patients in the dispensary (35 per cent as compared with 28 per cent). Cultures were obtained in 50 per cent of the cases which gave positive results microscopically. They were positive in 5 per cent of cases in which the microscopic observations were negative. As I recall it, seven different organisms were found, Epidermophyton interdigitale being the most common. The method of testing the scales used by the essayists is not perfect, but it has not been possible as yet to devise any method of testing for fungi which exactly parallels conditions in vivo. I am sorry that no further work has been done by Drs. Sharlit and Muskatblit, who last year reported a new method of testing the fungicidal action of chemicals.

Dr. Earl D. Osborne, Buffalo: I think that Dr. Templeton has brought out a great many important facts under discussion at present, as to both prophylaxis and treatment. The tests were done with Trichophyton interdigitale, which is the most common organism. On the other hand, it has been shown that Trichophyton rosaceum is twice as resistant to fungicides as the other fungi. This organism is so common in California that I think the tests should be done with the most resistant organism. In all our culture work with patients and students regarding the frequency of Trichophyton rosaceum as compared with Trichophyton interdigitale, the results were comparable with Dr. Weidman's.

In our study of the prophylaxis of ringworm we have followed a great many graduates of the Buffalo high schools through the first two years at the University of Buffalo. We should soon be able to evaluate the prophylaxis of ringworm by sodium hypochlorite. It is curious how many persons will be found to give positive results for ringworm on one occasion and show nothing clinically later. It seems to me that if we are going to judge the effect of drugs we must take into consideration the normal tendency for ringworm to clear up, at least clinically, of its own accord.

When we published our paper last year on the prophylaxis of ringworm the method had been in use one year among 15,000 high school students. Up to date in all Buffalo high schools there has not been a single new case of ringworm reported. There may be some new cases—I would be much surprised if there were not—but not a single new case has been brought to our attention among the high school students in Buffalo. I have also been checking up in private practice. During the past year we have not had a single new case of ringworm of the feet in a Buffalo high school student. I do not doubt that there are new cases, for

some of these students frequent gymnasiums other than those connected with the high schools of Buffalo, but apparently the prophylaxis with sodium hypochlorite is efficient.

Another thing is the matter of expense. Merthiolate and metaphen, although effective, are so expensive that their use is prohibited. I have had several patients who found it entirely impossible to continue treatment with these drugs because of this expense. The same thing applies to the prophylaxis of ringworm. Sodium hypochlorite is effective and cheap. In Buffalo the average expense is 17 cents a day per pan for prophylaxis.

Dr. C. Guy Lane, Boston: In the last two years we have been able to arouse some interest in the department of botany at Harvard in the matter of medical mycology. During the past year at the new Biological Institute a graduate student has been assigned to work on some of these problems with us, doing cultural work at the Institute and putting in part time work at the office. This year he has done some rather interesting work with soaps. Using Trichophyton interdigitale, he obtained a growth when a 4 per cent solution of soap had been incorporated in the agar. He also used five different organisms and showed that exposure to a 5 per cent solution of one of several different kinds of soap does not interfere with growth. Exposure to so-called germicidal soap, however, under the same conditions results in no growth. Exposure of Trichophyton asteroides to a 1:20 solution of sodium oleate, ivory soap and naphtha soap for forty-five hours gave positive cultures. This whole question of soap was raised by an industrial case in which the patient claimed to have obtained an infection by washing his hands in soapy water that had been used by another person who was proved to have a fungus infection of the hands.

Trichophyton interdigitale, when ground up in the form of an emulsion and mixed with distilled water, gave positive transplants for only six days, but transplants mixed with rain water gave positive cultures for thirty-six days. Unsterilized water gave positive cultures for seventy-eight days, and sterilized tap water gave positive cultures for one hundred and six days. It was felt that contaminants in unsterilized water prevented positive cultures for a longer period. Microsporon fulvum was also grown and reclaimed, in much the same way that Dr. Templeton has described, from cardboard, cotton, filter paper, toe-nails, feathers, paper and wool; at the end of forty days it was possible not only to regain the culture but actually to see the growth in several instances. I congratulate Dr. Templeton on the excellent work that he has done in this field.

Dr. Henry J. F. Wallhauser, Newark, N. J.: I should like to ask Dr. Templeton if he included copper sulphate in these tests. In a clinical experience in the treatment of dermatophytosis with this remedy over a period of years the results were almost uniformly successful, and a comparison with the remedies that he mentioned would be interesting.

Dr. George M. MacKee, New York: I have made no scientific experiments with sodium hypochlorite. While it has been established that it has great value as a prophylactic agent, my clinical experience has been so disappointing that I am led to ask for some advice. Perhaps I have used the drug incorrectly. I have been using a 0.5 per cent solution, which I understood was recommended by Dr. Osborne. Dr. Templeton, I think, recommended 1 per cent. I have been having my patients use a foot bath in the bedroom or bathroom. The solution is made fresh each week. The patients stand in the solution for at least fifteen seconds. The method in my experience has not prevented recurrences. The treatment costs not more than $1.00 per month. I shall now try a 1 per cent solution.

As far as cultures are concerned, we have been impressed with the necessity of making numerous plants.

Dr. Walter J. Highman, New York: I was much interested in the comparison of incidence among males and females, as reported by Dr. Templeton and corroborated by Dr. Weidman. Of course, the first thing that occurs to one is the susceptibility of the respective sexes. Another thing may occur which Dr. Templeton explained in the terms of old and new gymnasiums, but what Dr. Weidman said seems to negate Dr. Templeton's remarks. One thing that has not been mentioned in the discussion is the foot itself. The feet of young men are more often carriers of Trichophyton than those of young women. Boys in the colleges are not as cleanly as girls and do not take as good care of their feet. Certainly with the exacerbations of trichophytosis it is conceivable that the parasites are in loco, ready to become active. I think that one place they are likely to lurk is around and under the nails. I think the hygiene of the feet deplorable, and believe that the parasitology of the feet when there is no activity is what should be investigated.

Dr. Earl D. Osborne, Buffalo: In answer to Dr. MacKee's remarks, I should emphasize strongly that we do not believe that sodium hypochlorite is curative. After giving it a thorough trial I am convinced that it is a failure as a curative agent although its daily use will prevent flare-ups. The strength of the solution as a prophylactic is 1 per cent, which allows for some dilution in the foot bath. The solution should be changed not less often than every second day.

Dr. H. J. Templeton, Oakland, Calif.: I am absolutely in accord with the remarks of Dr. Highman and Dr. Weidman. As pointed out in our original article, several years ago, we believe that there are factors other than the gymnasium environment, which partially explains the higher incidence among male students. The shoes of men are heavier, causing their feet to perspire more freely. Many men wear wool hose while women wear sheer silk. We can grow Trichophyton interdigitale on wool socks, but it grows with difficulty on silk and not at all on cotton. This has been shown to be due to the nitrogen requirements of the fungus.

As to the expense of certain of the drugs, I should say that this factor would prohibit their use for foot baths but that they could be used locally.

We were familiar with Schamberg's work showing that Trichophyton rosaceum is the most resistant organism in his part of the country, and we have no doubt that it is. In our locality, however, we have shown that Trichophyton interdigitale is the most resistant, and consequently we used it as our test organism. You will remember that in Schamberg's recent work he found that iodine and mercury were the most highly fungicidal metals.

In germicidal soap we have both these ions occurring as mercuric iodide, and we would expect the results mentioned by Dr. Lane. We have not tried copper sulphate. We used copper oleate in a small group of students and were not impressed with the results. We have used sodium hypochlorite in the treatment of a group of 38 students, and agree with Dr. Osborne and Dr. MacKee that it was not of conspicuous value—certainly not of the value that it probably is when used as a prophylactic agent in foot baths.

ECZEMA DUE TO HYPERSENSITIVENESS TO RUBBER

A SCIENTIFIC STUDY

M. E. OBERMAYER, M.D.
CHICAGO

Dermatitis produced by contact with chemical substances used in the manufacture of ordinary rubber goods has been recognized for many years. Yet it is not generally known that ready-made rubber goods such as rubber gloves or condoms may give rise to eczema. The only case reported in the literature is that of dermatitis due to a rubber bunion protector.[1] The patient was sensitive to rubber bunion protectors only, not to gloves, corsets or garters. The bunion protector consisted of 90 per cent pure virgin rubber and of 10 per cent reclaimed rubber, and sulphur was used as a vulcanizer. Patch tests with other rubber products or sulphur were not made. In a case of hypersensitiveness to caoutchouc adhesive plaster as reported by Siemens [2] the offending agent was "Dammar-Säure," and not the rubber itself.

The following case of eczema due to cold-cured rubber has been studied in this clinic:

In a physician, aged 38, intense vesicular dermatitis first developed following sexual intercourse with the protection of a rubber condom. The dermatitis subsided in two weeks under treatment. Three years later acute eczema developed on the hands and wrists of this physician after he had worn rubber gloves. The eczema was more marked when the gloves were tight, and was aggravated by perspiration. Repeated use of rubber gloves produced a progressively more severe eruption.

He had had hay fever in a mild form since 1917. Since 1928, at the time of the onset of dermatitis from rubber gloves, there has been a yearly accentuation of the hay fever symptoms. Scratch tests in 1930 showed that he was sensitive to June grass, orchard grass, timothy, red top and large and small ragweed. Injection of polyvalent pollen extract practically cured the hay fever, but did not decrease hypersensitiveness to rubber. This is in accord with the experience of Hazen [3] and others.

A year after the appearance of the dermatitis of the hands due to rubber gloves, the condition became so severe that the patient found it necessary to wear cotton

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From the Division of Dermatology, Department of Medicine, University of Chicago.

Read before the section on Dermatology and Syphilology at the Eighty-Third Annual Session of the American Medical Association, New Orleans, May 12, 1932.

1. Niles, Henry D.: Dermatitis Due to Rubber Bunion Protector, J. A. M. A. **97**:778 (Sept. 12) 1931.

2. Siemens, H. W.: Hypersensitiveness to Ordinary Court-Plaster, Zentralbl. f. Haut- u. Geschlechtskr. **2**:426, 1921.

3. Hazen, H. H.: Allergic Dermatoses, Arch. Dermat. & Syph. **18**:121 (July) 1928.

gloves underneath. Whenever the wrist of the rubber glove was longer than that of the cotton glove, a ring of dermatitis developed about the wrist beneath the rubber. A severe vesicular eruption developed twice during 1931 when the patient absent-mindedly put on rubber gloves alone.

I undertook the problem of determining what the chemical irritant was and of endeavoring to counteract the action of this chemical agent. An attempt was made to transfer the hypersensitiveness to two normal persons by means of the Prausnitz-Küstner method (intracutaneous injection of the patient's blood, followed by application of rubber at the site of injection by the method of Urbach [4]), with negative results.

To understand the manifold possibilities of the problem, the following brief outline of the chief phases in rubber production is given.

The coagulated milky juice, as it is obtained from various tropical plants, is commonly called latex. Latex is composed entirely of carbon and hydrogen. Its chemical structure is not yet definitely known, but we do know that artificial rubber can be manufactured from isoprene (C_5H_8) by polymerization. On the other hand, if pale crêpe rubber is strongly heated, it breaks down into a number of simple liquid hydrocarbons, of which isoprene is one.

Before this crude rubber can be manufactured into rubber goods, it must be subjected to various chemical procedures. After being washed and treated with solvents (carbon bisulphide, benzene, mineral-naphtha and carbon tetra-chloride) it is subjected to the process of vulcanization, i. e., the heating of pale crêpe rubber with sulphur and zinc oxide. This is done in order to give the rubber the elasticity desired at various temperatures. Sulphur, when heated with pale crêpe rubber, combines fairly slowly. Certain chemical substances, called accelerators, hasten this process. When rubber is exposed to air and light, it slowly absorbs oxygen. To inhibit this process, anti-oxidants or inhibitors are added.

As one can see, a great variety of chemicals is employed in manufacturing rubber. Hence the reports from physicians taking care of the health of men working with rubber contain a vast number of cases of dermatitis due to external irritants. Dr. P. A. Davis of the Goodyear Rubber Company, who is chairman of the Section on Preventive and Industrial Medicine and Public Health of the American Medical Association, published a series of articles on the toxicity of substances used in the rubber industry. He informed me that most of the substances that were known to produce dermatitis have since been eliminated from the rubber industry in this country wherever possible. A comprehensive classification of the materials used in the rubber industry and their hazards to health was recently published by the National Safety Council.[5]

4. Urbach, E.: Hautkrankheiten und Ernährung, ed. 1, Vienna, Wilhelm Maudrich, 1931.

5. Compounding Materials Used in the Rubber Industry, Industrial Safety Series, no. ru. 1, Chicago, National Safety Council, 1931.

In many instances it is not the chemical substance itself but impurities which the commercial product contains that give rise to dermatitis. In the majority of cases the dermatitis was due to one of the accelerators. Accelerators that are well known causes of dermatitis are:

Hexa-nitro-di-phenylamine.[6] This is a powder, readily conveyed through the air. It was a constituent of German air-bombs and caused numerous cases of dermatitis in London in people who came in contact with the powder from unexploded bombs.[7]

Hexa-methylene-tetra-amine. Dermatitis caused by this accelerator is so common that it is sometimes called "rubber-itch." It is a definite irritant to most skins.[8a] The dermatitis is likely to develop among those workers who handle the warm, raw stock subsequent to the mixing operation, such as the warmers, the calendar-operators and sometimes the tire-builders. The dermatitis usually begins on the wrists and extends up the forearms, sometimes to the face and neck; in a few cases it becomes generalized. In some respects it resembles the eruption due to ivy-poisoning and is inclined to itch violently, especially at night. The dermatitis is not persistent, however, and disappears in a few days with change of occupation. According to Shepard and Krall,[9] the eruption is probably caused by the water-soluble hexa-methylene-tetra-amine entering the skin, where it is first decomposed and then oxidized in part to formic acid, the latter being the real cause of the dermatitis. On assumption that the acid of the perspiration is the primary cause of the decomposition, neutralization of this acid should prove an effective preventive measure, and if the irritant is formic acid, neutralization of this would prevent its action. Therefore treatment with a saturated solution of sodium bicarbonate was tried with success. Its effect was chiefly preventive, but also curative. Cole and Driver [10] also called attention to the irritating action of the products of decomposition in hexa-methylene-tetra-amine.

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6. Cleveland, D. E. H.: Dermatitis Venenata in the Rubber Tire Industry, Canad. M. A. J. **17**:637 (June) 1927; Weber, L. F.: A List of Cutaneous Irritants. Arch. Dermat. & Syph. **21**:757 (May) 1930.

7. Sequeira, J. H.: A Textbook of Diseases of the Skin, ed. 3, London, J. & A. Churchill, 1919, p. 86.

8. Davis, Paul A.: (*a*) On the Toxicity of Substances Used in the Rubber Industry, Rubber Age **26**:199 (Nov.) 1929; (*b*) **29**:367 (July) 1931; (*c*) **29**:461 (Aug.) 1931; (*d*) **25**:367 (July) 1929; (*e*) **25**:483 (Aug.) 1929; (*f*) **26**:431 (Jan.) 1929; (*g*) **26**:541 (Feb.) 1929; (*h*) **27**:367 (July) 1930; (*i*) **27**:477 (Aug.) 1930; (*j*) **28**:143 (Nov.) 1930; (*k*) **27**:145 (May) 1930; (*l*) **28**:27 (Oct.) 1930; (*m*) **28**:513 (Feb.) 1931, and (*n*) **29**:77 (April) 1931.

9. Shepard, N. A., and Krall, S.: Poisons in the Rubber Industry, J. Indust. Hyg. **2**:33 (May) 1920.

10. Cole, H. N., and Driver, J. R.: Industrial Dermatoses, J. Indust. Hyg. **4**:425 (Feb.) 1923.

Tri-ethyl-tri-methylene-tri-amine. This is a concentrated polymerized condensation product of formaldehyde and ethylamine.

Para-phenylene-di-amine. This is not a powerful accelerator; it is, however, used extensively in the dye industry and in the dyeing of hair and furs.[10]

Safex. This is a patented accelerator.

B. B. accelerator. This accelerator is a condensation product of butyraldehyde and di-methyl-para-phenylene-di-amine.

Methylenaniline. The commercial product often contains traces of uncombined aniline or formaldehyde, and the irritation is probably due to the latter.

Oxynone; para-nitroso-di-methyl-aniline. This substance may produce a vesicular dermatitis which shows a tendency to spread, and which sometimes becomes generalized. Later, exfoliation occurs. The dermatitis is extremely resistant to therapeutic measures. Animal experiments gave positive results.[8b]

Phenyl-beta-naphthylamine.[8c] This substance is toxic only to persons who are hypersensitive to it (about 3 per cent of normal people). In a few persons hypersensitiveness develops after some time has elapsed.

Of the solvents for latex already enumerated, benzene is the chemical most commonly mentioned as a cause of dermatitis.[8d] Carbon tetrachloride may also give rise to dermatitis.[8e]

Of other chemical substances used in the rubber industry, zinc and its compounds are injurious to the skin only in the case of the chloride and sulphate.[8f] Chromium and its compounds are common cutaneous irritants.[8g] Dermatitis has been reported as resulting from antimony [8h] and from arsenic.[8i] Only occasionally and in a mild form does dermatitis occur from the handling of guanidine compounds,[8j] and from acetone.[8k] Ethyl-acetate has likewise given rise to dermatitis.[8l] Last, but not least, sulphur is extensively used; therefore sulphur and its derivatives [8m] must be taken into consideration in any attempt to determine the etiologic agent in dermatitis due to rubber.

EXPERIMENTAL WORK

The first question to be answered was whether hypersensitiveness was due only to the finished goods or was caused by the raw material also. As a preliminary step, my associates and I applied patch tests of the following materials: (1) rubber gloves and (2) pale crêpe rubber (nonvulcanized rubber). While the former yielded a definitely positive reaction, no reaction was produced by the latter, which proved that the offending agent was formed during the process of manufacture.

Knowing this, the second logical step was a search for the responsible chemical substance employed in the manufacturing process. Dr. M. S.

Kharasch, Professor of Chemistry, University of Chicago, kindly assisted in this work. In accordance with what has already been said, the chemical irritants giving rise to a dermatitis could be classified as: (1) sulphur itself and various inorganic and organic sulphur compounds, (2) accelerators and (3) anti-oxidants.

In order to ascertain a possible hypersensitiveness to sulphur and to various oxidation and reduction products of this element, my associates and I applied patch tests of: (1) 5 per cent precipitated sulphur in petrolatum, (2) 1 per cent sodium sulphide, and (3) sulphurylchloride.

Furthermore, since in the process of vulcanization some sulphur derivatives are undoubtedly formed, we wished to ascertain whether the irritating effect was due to the presence of some organic sulphur compounds. For this reason the following well known compounds were tried: (1) para-thio-cresol, (2) sodium-di-methyl-di-thio-carbamate, (3) tetra-methyl-thi-uram-di-sulphide and (4) cystein.

All of these tests were negative. It is to be noted that two of the sulphur compounds applied, namely, sodium-di-methyl-di-thio-carbamate and tetra-methyl-thi-uram-di-sulphide, are also commonly used ultra-accelerators. Several substances of the mercaptan group, such as thio-glycollic acid and ethyl-mercaptan were refused by the patient because of the offensive odor.

With the sulphur compounds and accelerators thus eliminated, there still remained the possibility that the hypersensitiveness was caused by the anti-oxidants commonly employed. Therefore, tests were applied with: (1) di-phenylamine, (2) phenyl-alpha-naphthylamine and (3) phenyl-beta-naphthylamine.

They all proved to be negative. In all tests performed with liquids, concentrated alcohol was used as a control. The patch tests were applied in the usual way to the back of the patient and were removed after thirty-six hours.

With all these negative tests, the question naturally came up as to whether the patient actually was hypersensitive to ordinary rubber goods, or only to a specific rubber product. Hence sections of the following rubber products were tried: (1) rubber glove, (2) ordinary tire rubber, (3) ordinary rubber stopper, (4) ordinary rubber tubing and (5) synthetic rubber.

While glove rubber yielded a definite papulovesicular dermatitis, no reaction was produced by the other rubber products.

Since the sulphur, the sulphur compounds, the accelerators, the anti-oxidants and also, most surprisingly, the ordinary rubber articles themselves did not cause irritation, it became fairly evident that the primary cause of the dermatitis was a difference in the reagents employed in manufacturing ordinary rubber gloves and condoms as compared with

those employed for other rubber articles. While ordinary rubber goods such as automobile tires, stoppers, tubing, etc., are "hot-cured," as already briefly described, thin-walled articles like gloves and condoms are prepared at ordinary temperature. This "cold-curing" consists essentially of the following chemical process.

Sulphur-mono-chloride and zinc oxide are mixed in a certain percentage, and thin, crude sheet rubber is exposed to the action of the chloride of sulphur. Sulphur-mono-chloride is a well known chemical substance which possesses an extremely powerful and disagreeable odor; it is readily hydrolized by water and, since it decomposes so rapidly, is irritating to the mucous membranes and to the skin.

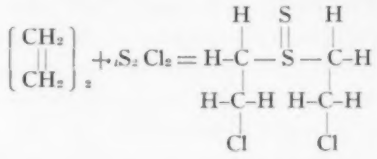
It was suggestive, therefore, that sulphur-mono-chloride, which is employed only in "curing" the goods to which the patient was sensitive, played an important part in inducing the eczematous reaction. Since it is well known that rubber cured by sulphur-mono-chloride gives an acid reaction to litmus, it was necessary to test the possibility that the sensitiveness was due to hydrochloric acid. This possibility was readily disposed of, however, by application of a patch test of a dilute solution of hydrochloric acid (2 per cent), which gave a negative result.

A direct test application of sulphur-mono-chloride was impossible because of the offensive odor of this substance, but even so, a negative test with pure sulphur-mono-chloride would not have been conclusive proof against it as a potential factor, because during the "curing process" chemical substances are undoubtedly formed, the effect of which is likely to be entirely different from that of the original substance. Therefore, crude sheet rubber was cured with sulphur-mono-chloride, and other crude sheet rubber also cured, but with chemical compounds not containing chlorine. Patch tests of the following products were applied: (1) rubber cured with sulphur-mono-chloride, (2) rubber cured with tepidone (a compound recently produced by the DuPont Company) and (3) rubber cured with pipsol.

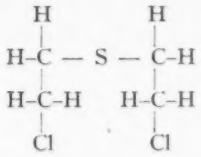
Tepidone and pipsol are new patented compounds which do not contain chlorine; they have been submitted to the trade for the cold-cure of articles such as rubber gloves and condoms. The first test was positive; the others, negative.

The conclusions one would reach from these observations would be that the irritant was some chemical compound formed by the combination of sulphur-mono-chloride with the unsaturated molecules of the crude rubber. This hypothesis receives some confirmation from the well known fact that sulphur-mono-chloride combines extremely rapidly with unsaturated compounds, in many instances producing powerful vesicant agents. Thus mustard gas, which was much dreaded during the World

War, since the slightest contact with it called forth severe burns, is formed by the action of sulphur-mono-chloride on ethylene.



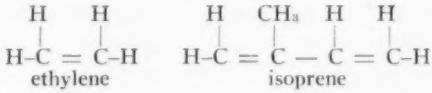
This substance readily loses its second sulphur and goes over into:



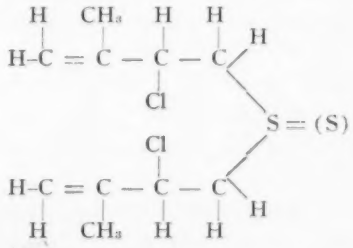
which is mustard gas.

The empiric formula of latex can be given, as briefly stated before, as isoprene (C_5H_8).

It has been stated by Paul A. Davis [8n] that the action of sulphur-mono-chloride on isoprene leads to the formation of a compound of the empirical formula $(C_{10}H_{10})_2S_2Cl_2$. While it is difficult to state the exact attachment of the carbon and sulphur and carbon and chlorine linkages in that molecule, it is nevertheless evident that if any attachment results in a compound similar to the one formed by the action of sulphur-mono-chloride on ethylene, the possibility of a substance possessing vesicant action is at once indicated. The analogy between ethylene and the mother substance of rubber, isoprene, is as follows:



While by the action of sulphur-mono-chloride on ethylene mustard gas is formed (as we have stated), the compound formed by its action on isoprene may be a substance of similar chemical structure:

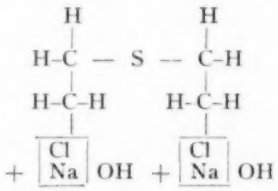


At the surface in most of the material thus formed the halogen probably is hydrolyzed and would therefore be a nonvesicant product.

If, however, in the layer underlying the surface the hydrolytic action has proceeded to a much lesser extent, it may by virtue of the vapor pressure of the material lead to irritation in particularly sensitive persons.

The choice is therefore whether the chlorine-sulphur-isoprene compound produced the irritation merely by its presence at the surface, or whether the material present in the inner layers also plays a part. This cannot be answered with available data.

Having solved the first part of the problem by determining the substance at fault and its probable chemical mechanism, it was next necessary to find a way of counteracting its irritant action. If mustard gas is treated with alkali, it is made into beta-beta-di-hydroxy-di-ethylsulphide.



The resulting substance has no vesicant action.

If the substance produced by the sulphur-mono-chloride in rubber has a similar structure, then the treatment with alkali should lead to destruction of irritant action similar to mustard gas. Therefore, pieces of rubber gloves were soaked in a 4 per cent sodium hydroxide solution for forty-eight hours. After that time the solution showed a slightly yellowish color and contained some suspended material. The filtrate, when acidified with nitric acid and treated with silver nitrate, gave a white precipitate of silver chloride; this was confirmed by dissolving the silver chloride in ammonium hydroxide and precipitating with nitric acid. This test indicates the presence of a labile chloride ion in the rubber cured with sulphur-mono-chloride. The fact that the filtrate, on acidification and treatment with silver nitrate, gave a white precipitate indicates the absence of sulphides in solution. Therefore, the attachment already postulated has actually taken place.

Thus, theoretically, the right method of procedure seemed to have been found. It was then necessary to verify these theoretical results on the patient. Patch tests were applied with: (1) ordinary rubber gloves and (2) rubber gloves prepared by soaking for forty-eight hours in a 4 per cent sodium hydroxide solution.

While the former yielded the same positive reaction as it had before, the latter showed no reaction.

Since that time the patient has used exclusively rubber gloves prepared according to the method stated. He wears them a great deal without the protection of cotton gloves beneath and has never had any sign of cutaneous irritation. The working hypothesis was thus substantiated.

I should like to call attention to the fact that Stokes [11] recommended treatment of rubber tubing used in various intravenous procedures by alkali in order to prevent the so-called "tubing reaction." The alkali treatment is supposed to remove sulphur and sulphides. The causes of the tubing reaction and of the dermatitis in the case cited are not identical, for two reasons. First, application of untreated rubber tubing to the patient's skin did not produce dermatitis. The differences in the manufacture of cold-cured and of hot-cured rubber must be kept in mind. Second, I believe that certain colloidal polysulphides are present in the rubber tubing, which would be removed by the alkali, obviating the "tubing reaction," which is in the nature of a so-called "colloidal reaction."

SUMMARY

The case of a physician is reported in whom vesicular eczema developed on contact areas following the use of rubber gloves or condoms.

The chemistry of the manufacture of rubber is presented briefly, and the substances employed which may give rise to a dermatitis are enumerated.

Studies made on the patient revealed that the hypersensitiveness was not due to: (1) crude rubber, (2) chemical substances employed in manufacturing ordinary rubber goods or (3) ordinary rubber goods themselves.

It was therefore assumed that the irritating agent was formed during the process of cold-cure vulcanization used in the manufacture of gloves and condoms.

While glove rubber cured with sulphur-mono-chloride gave a positive result, such material cured with substances not containing sulphur-mono-chloride gave a negative result. The chemistry of sulphur-mono-chloride was studied; the probable offending compound was postulated.

The similarity of the compound to mustard gas led to the idea of rendering it nonirritant by treatment with alkali. After the chemical experiment had verified the theory, treatment of rubber gloves with 4 per cent sodium hydroxide was tried. The result was gratifying, and the patient is now able to work with gloves treated with alkali without having dermatitis.

ABSTRACT OF DISCUSSION

DR. C. GUY LANE, Boston: Dr. Obermayer has presented the facts which he has traced by careful reasoning and chemical knowledge. He discovered the cause and developed the proper methods of treatment and prevention. He has exemplified the course one should pursue in all these dermatoses.

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11. Stokes, John H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1927, p. 177.

Dr. William A. Pusey, Chicago: I know of no case of external irritation which has been worked up so splendidly as the one reported by Dr. Obermayer, and which has responded so brilliantly to this therapy.

Dr. Clark W. Finnerud, Chicago: I wish to inquire of Dr. Obermayer whether or not a particular compound was included in his list. In patients with a chronic dermatitis, which was diffuse over the face and neck chiefly, but also occurred on the hands and forearms, we found that the irritant was a new preparation used in finishing rubber products, an accelerator used in curing rubber for vulcanizing. This was a yellow powder caller dinitrophyl-dimethyl-dithiocarbomate.

Dr. Fred D. Weidman, Philadelphia: In Dr. Obermayer's presentation, I was struck by the way in which the particular sulphur compounds employed were led over into the formula of mustard gas.

Dr. Everett S. Lain, Oklahoma City: Had any members of the dental profession been present today and heard these discussions, they would have been first amused and then edified. For a long time they have had under discussion troubles in the mouth caused by the use of rubber as a basic dental material. They are of the opinion that there is a possibility of irritation to the oral mucosa by mercuric sulphide, which gives the rubber the red appearance, also by sulphur which is used for hardening. They have concluded that most of the trouble is due to lack of proper curing. Many dentists recommend that dental plates be immersed in soda water during the night. They have learned by experience that it keeps them in better condition. I have learned that this irritation is more likely to occur in a mouth that is excessively acid rather than alkaline. Dr. Obermayer has offered the reason for the benefit of soaking the plates in an alkaline solution. This mitigates the danger of injury from the free sulphur which is sometimes contained in vulcanite dentures.

I thank Dr. Obermayer for his solution of this problem which had puzzled those of us who have been working with stomatitis caused by artificial dentures.

Dr. Earl D. Osborne, Buffalo: I wish to express great admiration for Dr. Obermayer's scientific work in eliciting the exact cause of the dermatitis following contact with rubber. In our paper I called attention to the series of cases of dermatitis following the use of certain rubber gloves by the Niagara Hudson Corporation. One workman was markedly sensitive to the rubber. This rubber was soaked in 4 per cent sodium hydroxide for forty-eight hours. Later some of the rubber was soaked in 20 per cent sodium hydroxide for forty-eight hours and then thoroughly washed in running water, and still the patient reacted.

Dr. M. E. Obermayer, Chicago: The concentration of substances used for patch tests should be standardized. Not only would this give more uniform results, but the results of the various investigators could be better compared and evaluated. Recently a paper was published from Jadassohn's Clinic which gave the concentrations of a large number of irritants. I feel that a similar standard concentration chart would be of value for the work in this country.

In answer to Dr. Finnerud's question I might state that the chemical substance mentioned by him has not been recorded by me, but its action is practically identical with that of one of the accelerators mentioned in my list. This substance should also be considered a possible irritant in rubber.

I agree with Dr. Lain's statement, and I feel that because of the great variety of the end-products in the rubber industry there may be a different chemical agent responsible for the various forms of eczema due to rubber preparations. This last point seems important. It was shown in my paper that in testing patients for hypersensitiveness to commercial substances one has to be certain first that the test material actually contains the suspected substance. Just as in my case testing with rubber which had been prepared without sulphur monochloride would not have yielded any results, it is quite likely that other commercial substances may be manufactured in various ways which chemically differ entirely. In every case of hypersensitiveness it is important to procure the test material from the same source and to ascertain that the manufacturing process has not been changed.

GOLD DERMATITIS LIMITED TO DEPIGMENTED SKIN

WITH A THEORETICAL CONSIDERATION OF ITS ETIOLOGY

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The unusual phenomenon of gold dermatitis limited to depigmented skin has recently been observed in two cases. In both cases the dermatitis followed injections of gold sodium thiosulphate administered in carrying out the treatment for vitiligo recommended by Lindsay.[1] We believe that this cutaneous accident is of interest because it represents a hitherto undescribed reaction to gold compounds, because the limitation of any dermatosis to depigmented skin is an unusual phenomenon and because a consideration of the possible mechanism involved may assist in an understanding of two common dermatoses, vitiligo and aurodermatitis.

While the classic studies of Bloch,[2] which have been elaborated in this country by Becker [3] and by Peck,[4] have furnished much more exact means of studying pigment formation in the skin and have shown that the fundamental change in vitiligo is an absence of dopa-oxydase, the underlying etiologic agent remains unknown. Bloch [5] has summed up the cause for its development in the term *"Aufbrauchsdermatose,"* exhaustion dermatosis, in which the dopa-oxydase is lacking because of the action of some undetermined stimulant or toxic agent.

The physiologic action of gold on the skin is likewise unknown, although the general similarity of its reactions to those of other heavy

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1. Lindsay, H. C. L.: Treatment of Leukoderma with Gold Sodium Thiosulphate, Arch. Dermat. & Syph. **20**:22 (July) 1929.

2. Bloch, B.: Das Pigment, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1927, vol. 1, pt. 1, p. 431.

3. Becker, S. W.: Melanin Pigmentation: A Systematic Study of the Pigment of the Human Skin and Upper Mucous Membranes, with Special Consideration of Pigmented Dendritic Cells, Arch. Dermat. & Syph. **16**:259 (Sept.) 1927.

4. Peck, S. M.: The Melanotic Pigment in the Skin, Hair and Eye of the Gray Rabbit, Arch. Dermat. & Syph. **23**:705 (April) 1931.

5. Bloch, B.: Zur Pathogenese der Vitiligo, Arch. f. Dermat. u. Syph. **124**: 207, 1917.

metals and its distribution on injection have been studied by Brown, Saleeby and Schamberg,[6] Lomholt[7] and others. The variety of reactions of the skin to gold compounds is seen to be widening constantly, and adequate summaries are available in the papers of Lebeuf and Mollard,[8] Driver and Weller[9] and Throne, Kingsbury and Myers.[10] In our cases, unlike any reactions previously reported, there is demonstrated a peculiar predilection for skin in which a known physiologic dysfunction, failure of melanogenesis, was present. We believe that a logical theory of this remarkable selectivity of reaction can be advanced.

REPORT OF CASES

CASE 1.—A. H., a girl, aged 14, weighing 47.7 Kg., well developed and well nourished, of German descent, was first seen on July 16, 1929. She presented extensive patches of vitiliginous depigmentation distributed over the entire body. A few lesions on the back were centered by small brownish-black nevi. There was moderate hyperpigmentation at the margins of the depigmented spots.

General examination revealed no systemic abnormalities. The Kolmer, Wassermann and Kahn reactions of the blood were negative. The vitiligo began on the back within a month after the administration of diphtheria antitoxin (?) in 1922, and since that time there had been constant gradual enlargement of the old lesions and appearance of new patches. It was not known whether the original lesions appeared about nevi. There were no subjective symptoms. No undue exposure to sunlight or the appearance of other cutaneous lesions preceding the onset of the vitiligo was recalled by the patient's father. The depigmented areas were stated to have shown a greater reaction than the normal skin on exposure to sunlight. The pigmented skin showed normal tanning on the exposed surfaces during the summer months. The patient's general health had always been excellent, and there was no evidence or history of endocrine dysfunction.

The father of the patient also presented an extensive vitiligo of the trunk and arms which he stated developed following a severe febrile reaction to typhoid vaccine given in 1918. The patient's mother and brother had no pigmentary changes of the skin. All members of the family were of the Nordic, blond, blue-eyed type.

Following the suggestion of Lindsay,[1] treatment with gold sodium thiosulphate was begun on July 31, 1929, when 30 mg. was given intravenously. Gradually increasing amounts were administered at weekly intervals, and on September 10, the dose had reached 100 mg. Following each succeeding dose a moderate ery-

6. Brown, Herman; Saleeby, E. R., and Schamberg, J. F.: Study of Toxic Effects of Certain Gold Compounds, as Indicated by Blood Chemistry and Pathologic Changes in Organs, J. Pharmacol. & Exper. Therap. **28**:141 (July) 1926.

7. Lomholt, S.: Die Zirkulation des Goldes bei der Sanocrysin Behandlung, Biochem. Ztschr. **172**:141, 1926.

8. Lebeuf, F., and Mollard, H.: Morphologie des aurides, essai de classification, Ann. de dermat. et syph. **7**:214, 1931.

9. Driver, J. R., and Weller, J. N.: Untoward Results from the Use of Gold Compounds, Arch. Dermat. & Syph. **23**:87 (Jan.) 1931.

10. Throne, B.; Kingsbury, J., and Myers, C. N.: Unusual Clinical Manifestations Following Intravenous Administrations of Gold Compounds, Arch. Dermat. & Syph. **25**:494 (March) 1932.

thema of the depigmented areas was seen, developing within four hours after the injection and persisting for twenty-four hours. There was no evidence of pigment deposition in the vitiligo.

On September 30, the patient presented slight scaling and erythema of the vitiliginous patches over the elbows. The dosage of the gold compound was reduced to 50 mg. Seven days later, at which time a total of 765 mg. of gold sodium thiosulphate had been administered in ten weekly injections, the patient presented herself, showing an erythematosquamous dermatitis of practically all the areas of depigmentation, an exfoliative cheilitis with moderate edema and a scratch impetigo

Right shoulder, showing papulosquamous eruption with superficial fissuring (case 1).

of the forearms and chin. The normal pigmented skin of the trunk, upper arms and legs was unchanged, no scaling or erythema being visible. The mucous membranes of the mouth and vulva and the conjunctiva were normal. The subjective symptoms were mild, consisting of moderate pruritus of the affected areas of skin and some discomfort about the lips incident to the edema. The temperature was normal, and there was no lymphadenopathy.

Under treatment with ammoniated mercury ointment the impetigo improved rapidly. The dermatitis continued to increase in severity for two weeks, the scale becoming heaped up, and painful fissures developed about the knees and wrists. Urinalysis, made on November 8, showed no albumin, sugar or casts. Complete

examination of the patient's skin and mucous membranes revealed that none of the vitiliginous patches had escaped dermatitic changes, which varied from moderate erythema and slight scaling to a dusky red suffusion and thick, heaped-up, grayish-white scaling. The scale was psoriasiform and tended to be most marked toward the center of the depigmented patch. An outstanding feature of the process was its extreme dryness; there were neither vesicles nor true crusting.

Exposure of a portion of the dermatitis to an erythema dose of ultraviolet rays did not seem to aggravate the process. Under alternate applications of an ichthyolated zinc oxide ointment and a tar distillate ointment the dermatitis involuted slowly, but was still present on December 10, when the patient was seen for the last time. A communication from the father the following spring stated that complete involution did not occur until in March, 1930, and that no return of pigment was noted.

CASE 2.—L. M., an intelligent mulatto, aged 26, a trained nurse, presented an extensive vitiligo of fourteen years' duration. The depigmentation affected principally the face, neck and upper arms, but there were a few patches about the waist and over the thighs. The patient stated that she had observed a return of pigment in a few lesions. Her general health was excellent, and there was no history of serious illness. The family history showed no vitiligo or evidence of allergy. General physical examination of the patient revealed no abnormalities other than vitiligo; the Wassermann reaction of the blood was negative, and the urine was normal. At the age of 16 years the patient had received from thirty to forty injections of neoarsphenamine for the vitiligo, which were without effect and produced no toxic reactions. A Wassermann test of the blood was not done previous to the injections.

The patient was given gold sodium thiosulphate intravenously, the initial dose being 25 mg. Between Feb. 17, 1931, and May 5, she received 700 mg., divided into eleven doses. Following the suggestion of Maloney,[11] who thought that the good results in Lindsay's case might have been in part dependent on the patient's residence in a sunny region, suberythema doses of ultraviolet rays were given twice weekly. The patient's veins were almost inaccessible, and on two occasions, at least, there was leakage of a few drops of the gold solution. This produced no local reaction or visible discoloration. Following every injection after the fourth the patient stated that some erythema was noted in the depigmented patches, developing within a few hours and lasting several days. This reaction persisted after the exposures to ultraviolet rays were discontinued following the seventh injection of gold sodium thiosulphate. There were no subjective symptoms associated with the erythema.

Following the injection of 100 mg. of gold sodium thiosulphate on May 5, there were seen, on May 26, the remains of a dry scaling erythema of the depigmented patches that had appeared two days after the injection. The patient believed that some return of pigment was occurring in a vitiliginous lesion on the neck and was anxious to continue therapy. Accordingly, another dose of 50 mg. of gold sodium thiosulphate was administered on May 26. One week later an erythematous, large, flat, diffuse, maculopapular eruption, limited to the vitiliginous areas over the abdomen, chest and back, was noted. There was no exudation. Scattered through the eruption were a few large, flat, inflammatory papules. These resembled, somewhat, a papular pityriasis rosea. When the patient was seen again a week later, on June 9, the eruption had increased slightly, being still limited to the vitiliginous

11. Maloney, E., in discussion of Bechet, P.: Leukoderma Treated with Autotherapy Followed by Dermatitis, Arch. Dermat. & Syph. **21**:507 (March) 1930.

areas. The papular phase of the eruption was always seen at the center of a vitiliginous patch, with gradual fading of the dermatosis toward the periphery of the depigmented area. In no case were any inflammatory changes demonstrable within from 0.5 to 1 cm. of the periphery of the lesion, and no changes were noted in normal pigmented skin. The subjective symptoms were mild, consisting of moderate itching and slight burning of the affected patches. Urinalysis was negative for albumin, sugar and casts, and a blood smear contained 2 per cent eosinophils.

A piece of tissue was removed from a lesion on the back on June 30. It was examined histologically by Dr. Fred D. Weidman, whose report was as follows: The epidermal changes consisted of metaplasia of the basal cells into prickle cells. The basement membrane was indefinite by reason of edema affecting the epiderm and papillae. The outstanding change in the section was confined to the most superficial parts of the corium. It consisted of edema of a singular droplike character, lending a honey-combed appearance to the papillae. There was moderate hyperplasia of the fibrous tissue cells and moderate infiltration of lymphoid cells and a few polymorphs. There was no fibrin. Red blood cells appeared consistently throughout the section in the same superficial distribution, for the most part fused into small and larger masses, which showed more intensely pink than ordinarily. There were no granules as of gold. There was an absence of melanin in the basal cells. No degenerative changes were seen in the walls of the vessels. In summary, he said there was rather frank, severe, diffuse inflammation with numerous minute hemorrhages, limited strictly to the papillae and subpapillary parts.

The patient was lost sight of for a time, but was located in New York five months later. At that time patch and intradermal tests with a 20 per cent solution of gold sodium thiosulphate were performed. These were applied to both normal pigmented skin and depigmented skin that had previously been the site of the dermatitis. No reaction was noted to the patch tests. The site of intradermal injection of 0.1 cc. of 20 per cent gold sodium thiosulphate showed a definite reaction in twenty-four hours. This was slightly more marked in the depigmented skin, consisting of an inflammatory papule about 1 cm. in diameter, surmounted by a small tense vesicle. In the pigmented skin the reaction consisted of a similar papule without vesiculation. No pigmentation was noted following the involution of these lesions. The reaction was slightly more marked in the depigmented skin, but no significance was attached to this variation.

Control percutaneous and intradermal tests with 20 per cent gold sodium thiosulphate were performed on two subjects. In a normal subject with no pigmentary or other dermatoses, percutaneous tests revealed no reaction, while the intracutaneous test showed an inflammatory papule 0.7 cm. in diameter. This required four days for complete healing and left faint pigmentary remains, which have persisted for five months. In a young woman with an extensive vitiligo of ten years' duration similar tests were performed on pigmented and unpigmented skin. In this case duplicate intracutaneous injections were made and the sites of half the injections subjected within half an hour to an erythema dose of ultraviolet rays. This was done to determine whether light had any influence in increasing the sensitivity to gold sodium thiosulphate. An inflammatory papule was noted at each site of intracutaneous injection in twenty-four hours, but there was no variation in the pigmented or unpigmented skin nor in the region that had been exposed to ultraviolet rays.

After repeated efforts with slight variation in technic, we have been able to demonstrate gold in sections of skin taken from the second case. Of the methods available for the demonstration of gold in tissues, those of Christeller [12] and of Coquin [13] seem to have the widest application. The former is recommended by Okkels [14] and consists in the precipitation of gold in a strong hydrochloric acid solution of 5 per cent stannous chloride and is based on the long-known "purple of Cassius" [15] reaction of qualitative chemistry. A variation of the method includes preliminary exposure of the sections to strong sunlight. The method of Coquin consists of incineration of the specimen (from 2 to 3 Gm.), heating with a few drops of hydrochloric acid, evaporating to dryness and igniting. The presence of gold is determined by a purple color in the flame on ignition of the residue. This method has been modified by Patterson.[16] Wigley [17] stated that the procedure will detect traces of gold as small as 0.001 mg. present in tissue. Because of the small amount of tissue available in our case, we were unable to employ this method.

We have employed the stannous chloride method as follows: Formaldehyde-fixed, cleared sections were exposed to a "sunlight" lamp (S-1 bulb) for two hours and then were placed in a 5 per cent solution of stannous chloride containing approximately 2 per cent hydrochloric acid. The sections were left in the dark at 56 C. for forty-eight hours and were mounted in balsam without counterstaining. A positive reaction for gold was noted in the form of small, conglomerate masses sparsely scattered through the tissue which, on examination under oil immersion with careful adjustment of light, had a definite purple color and were composed of amorphous granules. Variations in technic in the form of omitting preliminary treatment of the sections with light and treatment of the sections with stannous chloride at lower temperatures for periods of time ranging from twenty-four to ninety-six hours failed to detect the presence of gold.

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12. Christeller, E.: Ein mikrochemischer Goldnachweis im Gewebe, Verhandl. d. deutsch. path. Gesellsch. **22**:173, 1927.

13. Coquin, R.: Researches de l'or dans les milieux organiques, Compt. rend. Soc. de biol. **43**:584, 1925.

14. Okkels, H.: Détection histochimique de l'or et du plomb, Compt. rend. Soc. de biol. **102**:1089, 1930.

15. Mellor, G.: A Comprehensive Treatise on Organic and Theoretical Chemistry, New York, Longmans, Green & Co., 1923, vol. 3, p. 564.

16. Patterson, quoted by Wigley, J. E. M.: Some Observations on the Deposition of Gold in the Skin, Brit. J. Dermat. **44**:69 (Feb.) 1932.

17. Wigley, J. E. M.: Some Observations on Deposition of Gold in the Skin, Brit. J. Dermat. **44**:69 (Feb.) 1932.

Formaldehyde-fixed sections were treated with 1 per cent solution of silver nitrate as outlined by Bloch,[2] followed by treatment with a saturated solution of sodium thiosulphate. No pigment-containing cells were demonstrated.

COMMENT

The various clinical manifestations of intolerance to gold compounds recently reviewed by Driver and Weller [9] and Throne, Kingsbury and Myers [10] may be summarized briefly. In general, the reactions are similar to those seen following the administration of other heavy metals, such as arsenic, bismuth, mercury and lead. Instances of extreme idiosyncrasy are relatively infrequent. While certain predisposing factors may exist, it would seem that the majority of the reactions are due to the toxicity of the gold compounds per se, and Hansborg [18] has pointed out that cumulative effects resulting from slow elimination of the drug or too large doses often result in toxic reactions. Throne and his co-workers [10] expressed the belief that a characteristic picture seen in metallic retention, namely, reduction of the blood chlorides and increase in the blood sugar, commonly accompanies the toxic manifestations following aurotherapy.

It would seem that little of the injected gold is deposited in the skin. The distribution is that seen with heavy metals, large amounts in the kidneys and liver, with much reduced quantities in the spleen, pancreas, heart and lungs (Lomholt,[7] Henius and Weiler [19]). Eichelberger and McCluskey [20] have shown that in normal and in tuberculous dogs an average of 50 per cent of the injected gold is excreted in the urine in from eighteen to thirty days. Impairment of renal function, as a result either of previous kidney damage or of the toxic metal damaging the normal kidney, may diminish the excretion of gold compounds.

Cases indicating some tendency toward residual pigmentation following aurodermatitis have been reported. The apparent dependence of this reaction on the effect of light has been noted in some instances. Kiess [21] has reported a case of gold dermatitis simulating pityriasis rosea in which there was marked residual pigmentation. Wigley [17] noted marked pigmentation in two of his cases of aurodermatitis, in

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18. Hansborg, H.: Fate of Elimination of Gold During Sanocrysin Treatment, Ugesk. f. læger **87**:725 (Aug. 20) 1925.

19. Henius, K., and Weiler, G.: Die quantitative Verteilung des Goldes in den Organen gesunder und tuberculöser Kaninchen nach Behandlung mit Goldpräparaten, Biochem. Ztschr. **214**:204, 1929.

20. Eichelberger, L., and McCluskey, K. L.: Effect of Injections of Sanocrysin on Normal and Tuberculous Dogs, Am. Rev. Tuberc. **14**:533 (Nov.) 1926.

21. Kiess, O.: Ueber eine der Pityriasis rosea ähnliche unter Pigmentierung abheilende Gold- (Aurophos-) Dermatitis, Dermat. Wchnschr. **86**:133 (Jan. 28) 1928.

one of which gold was demonstrated in the pigmented skin thirty-nine days after the last injection of a gold compound. Zimmerli and Lutz [22] have reported an argyria-like pigmentation occurring two years after a dermatitis developing during a course of injections of sodium aurothiosulphate. The pigmentation was most intense in the regions exposed to light. Gougerot and Carteaud [23] cited an instance of reticulated pigmentation subsequent to an erythroderma due to a gold compound which was most marked in areas exposed to light. Jäger, Kohl and Brunotte [24] and Hansborg [25] have observed generalized melanodermas following cutaneous reactions to gold compounds. Beaumont [26] and Savey [27] have described instances of a peculiar cyanotic blue discoloration of exposed skin following the use of sodium aurothiosulphate. Localized permanent bluish discoloration of the skin at the site of extravenous injections of colloidal gold has been reported by Schamberg.[28]

A case of dermatitis following aurotherapy for vitiligo has been reported by Bechet.[29] In this case the erythematous vesiculobullous dermatitis at first seemed more pronounced in the depigmented areas, but quickly became uniformly severe over the entire body. Bechet stated that the case represented the only severe reaction to gold compounds that he had encountered, despite his extensive experience with the drug in lupus erythematosus.

Examination of the various theories of the development of vitiligo in an effort to correlate a possible underlying physiologic dysfunction with the reaction observed in our cases has revealed little suggestive information. The wide variety of conditions that have been described as preceding the onset of vitiligo is striking. These include particularly syphilis, leprosy, psoriasis, pityriasis rosea, fungus infections, dermatitis venenata from various sources and light reactions. Lindsay [1]

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22. Zimmerli, E., and Lutz, W.: Eine eigenartige Form von Pigmentierung nach Goldbehandlung, Arch. f. Dermat. u. Syph. **157**:523, 1929.

23. Gougerot, H., and Carteaud, A.: Pigmentation réticulée survenue après une érythrodermie aurique, Bull. Soc. franç. de dermat. et syph. **38**:47 (Jan.) 1931.

24. Jäger, B.; Kohl, F., and Brunotte, H.: Grundsätzliche Erwägungen im Anschluss an einen Fall von Golddermatitis (Triphal), Arch. f. Dermat. u. Syph. **154**:76, 1927.

25. Hansborg, H.: Behavior of Gold in Organism After Intravenous Injections of Some Complex Gold Compounds, Bibliot. f. læger **121**:564, 1929.

26. Beaumont, G.: Sanocrysin, Sunlight and the Skin, Brit. M. J. **2**:818 (Nov. 3) 1928.

27. Savey, F.: Sanocrysin, Sunlight and the Skin, Brit. M. J. **2**:962 (Nov. 24) 1928.

28. Schamberg, J. F.: Chrysoderma: A Permanent Gold Staining of Skin, Arch. Dermat. & Syph. **18**:862 (Dec.) 1928.

29. Bechet, P.: Leukoderma Treated with Aurotherapy Followed by Dermatitis, Arch. Dermat. & Syph. **21**:507 (March) 1930.

has commented on the preponderance of involvement of exposed areas in an early case of leukoderma. Juster [30] has reported vitiligo following exposure to ultraviolet rays.

It is clearly evident that the local formation of some stimulating or toxic agent, which Bloch [5] predicated as the essential agent in the failure of melanogenesis, may arise as the result of numerous relatively unrelated disturbances. Since most of the suggested methods of treatment for vitiligo are based on methods involving stimulation of an already exhausted physiologic function of the skin, the almost universal failure of these varying therapeutic methods is not surprising. With [31] has reported indubitable evidence of return of pigment in a case of vitiligo exposed to the Finsen light, and Stein [32] reported some success following stimulation with carbon dioxide snow or exposure to the Kromayer lamp. Kissmeyer [33] stated that return of pigment practically always begins in small islands near the periphery of the lesion, and in one instance he believed that migration of pigment cells from the periphery was evident in dopa-stained sections. Preliminary photosensitization with various substances before exposure to ultraviolet rays is mentioned in some reports. Freund [34] first employed oil of bergamot in vitiligo, and Uhlmann [35] has reported a case in which this method was used successfully. Nadel [36] suggested the administration of acriflavine hydrochloride in conjunction with light therapy, and Irisawa [37] injected trypaflavine as a photosensitizer.

Instances of the occurrence of a dermatosis in a preexisting vitiligo are not numerous. In 1894, Welander [38] described his oft-cited case of vitiligo, lichen planus and neurodermite developing after a severe

30. Juster, E.: Apparition de plaques de vitiligo à le suite d'une érythème par rayons ultra-violets, Bull. Soc. franç. de dermat. et syph. **34**:111 (Feb.) 1927.

31. With, C.: Studies on the Effect of Light on Vitiligo, Brit. J. Dermat. **32**:145, 1920.

32. Stein, R.: Ueber experimentell erzeugtes Pigment im Vitiligo, Arch. f. Dermat. u. Syph. **97**:163, 1909.

33. Kissmeyer, A.: Studies on Pigment with the Dopa Reaction Especially in Cases of Vitiligo, Brit. J. Dermat. **32**:156, 1920.

34. Freund, R.: Ueber die Wirchungsweise des Solganal beim chronischen Infektion: Heilung des Goldexanthems durch Gold, Klin. Wchnschr. **6**:903 (May 7) 1927.

35. Uhlmann, E.: Pigmentbildung bei Vitiligo, Med. Klin. **23**:279, 1927.

36. Nadel, A.: Therapy of Vitiligo by Photo-Sensitization by Exposure to Ultraviolet or Sunlight with Simultaneous Administration of Acridine in Aqueous Solution, Acta dermat.-venereol. **11**:141 (April) 1930.

37. Irisawa, T.: The Treatment of Vitiligo by Phototherapy After Rendering the Patient Light Sensitive, Jap. J. Dermat. & Urol. **31**:1 (Jan.) 1931.

38. Welander, E.: De vitiligo, de lichen ruber planus, et de neurodermite chronique circinsente, Ann. de dermat. et syph. **5**:645, 1894.

nervous shock. The lichenoid eruption was confined to the patches of vitiligo. Shortly afterward, Neisser [39] demonstrated before the Fourth German Dermatological Congress a case of lichenoid eruption of the trunk and thighs developing in patches of long-standing vitiligo. The increased sensitivity of depigmented skin to light rays is a matter of common observation, and cases of lichenified dermatitis occurring in vitiligo on exposed portions of the body have been described by Weinberger.[40]

The intriguing possibility of differences in the sensitivity of pigmented and nonpigmented skin has been investigated by Kreibich,[41] following his observation of a case of eczema of the neck in a young girl with vitiligo in which the dermatitis was confined to the pigmented skin, and a case of psoriasis in which there was marked predilection of the dermatosis to pigmented rather than nonpigmented skin. He compared the reaction of pigmented and nonpigmented skin to croton oil and concluded that pigmented skin is more sensitive. Schultz [42] attempted a similar study, using varying dilutions of phenol as an irritant, but did not confirm Kreibich's observations, two of five cases of vitiligo showing increased reaction in the depigmented skin.

Hanawa [43] subjected the results of Kreibich and Schultz to critical evaluation and extended the scope of the study to animals. He confirmed Kreibich's conclusion that depigmented skin in man is less irritable than pigmented skin, using croton oil, cantharides, carbon dioxide snow and tincture of iodine as test substances. He criticized Schultz' use of phenol for determining sensitivity. Hanawa noted no difference in sensitivity between normal pigmented skin and smooth nevi. He found that the white skin of animals reacts less violently and heals more quickly after irritation and after infection with staphylococcus, streptococcus, cowpox and trichophytin. It is noteworthy that the reaction to gold compounds in our cases was in exact opposition to the foregoing observations, the supposedly more irritable pigmented skin remaining completely free from any dermatitic change.

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39. Neisser, A.: Ueber Vitiligo mit lichenoides Eruption, Verhandl. d. deutsch. dermat. Gesellsch., 1894, p. 435.

40. Weinberger, F.: Sommerprurigo und Vitiligo, Dermat. Wchnschr. **89**: 1332, 1929.

41. Kreibich, C.: Weitere Beiträge zur abnormen Hautempfindlichkeit, Arch. f. Dermat. u. Syph. **108**:41, 1911.

42. Schultz, I.: Beiträge zum klinischen Studium und der quantitativen Prüfung der Hautreaktion auf chemische Reige, Arch. f. Dermat. u. Syph. **113**: 987, 1912.

43. Hanawa, S.: Ueber die Beziehungen der Reizbarkeit der menschlichen und tierschen Haut zu ihrem Pigmentzinholt, Dermat. Ztschr. **20**:761, 1913.

Other evidence of differences in the physiology of pigmented and nonpigmented skin is seen in the experiments of Blazsó [44] and of Königstein.[45] Königstein found that white skin absorbs iodine from iodine salve or sodium iodide solution more rapidly than pigmented skin in animals. Blazsó [44] found marked differences in autolysis of pigmented and unpigmented skin at the same p_H. The increase in the autolysis of pigmented rabbit skin at p_H 3.8 was 300 per cent as compared to that of unpigmented skin. Similar differences were found in comparing autolysis of skin from different animals as well as of that of the same animal. These important studies lack confirmation so far as we are aware.

Woronoff [46] has recently described a method by which the reduction of silver nitrate by pigmented skin may be demonstrated clinically. Woronoff's method consists in laying a strip of filter paper moistened with 5 per cent silver nitrate so that a portion of the paper is in contact with both the pigmented and the unpigmented skin. On exposure of the region to light for several minutes, it is noted that the silver nitrate that is in contact with the pigmented skin is reduced, while the affected portion of unpigmented skin remains unchanged. This method is a simple corollary of the reduction of silver nitrate by pigmented skin seen histologically. We have repeated Woronoff's experiment in case 2 and obtained a similar result. The rapidity with which pigmented skin reduces silver nitrate following contact with the stratum corneum offers a most interesting demonstration of the effect of melanin or, as Woronoff suggests, its "decomposition products" on a photosensitive chemical.

Bloch [2] stated that other metallic salts may be reduced by melanin. These include gold chloride, osmium tetroxide and mercury salts. A possible influence of pigment on the gold salts deposited in the skin of our patients seems to us not unlikely. Assuming an equal rate of deposition of gold in pigmented and unpigmented skin in our cases, it seems possible that subsequent variation in the reduction or elimination of the gold from the skin might be influenced by the presence or absence of melanin. The nature of the chemical changes which gold salts undergo in the tissues is not known, but it is evident that they are one of a limited group of compounds on which melanin has a marked influence. We submit, therefore, the theory that the gold which was deposited in the unpigmented skin of our patients was reduced and

44. Blazsó, S.: The Difference of Autolysis in Pigmented and Non-Pigmented Skin of Animals, Magyar orvosi arch. **32**:209, 1931.

45. Königstein, H.: Reaktionsunterschiede zwischen gefärbter und ungefärbter Haut, Arch. f. exper. Path. u. Pharmakol. **97**:262, 1923.

46. Woronoff, D. L.: Die Silberreaktion an der Hautoberfläche bei Vitiligo und bei anderen Pigmentationsstörungen: Reflexionen über die erhölte wie herabgesetzte Sensibilität bei Vitiligo, Dermat. Wchnschr. **90**:105 (Jan. 18) 1930.

eliminated more slowly than that deposited in normal pigmented skin, and that this gold, through the cumulative effect of which Lomholt speaks, produced irritative effects limited strictly to the depigmented skin.

We do not believe that the irritative effects in our cases can be ascribed to light. In the first case there was an equal reaction to the gold solution in the exposed and unexposed areas of the cutaneous surface, and in the second case, although exposures to ultraviolet rays were employed as an adjuvant means of treatment, the reaction was much less severe than that noted in the first case. Moreover, exposure to strong ultraviolet rays after the dermatitis developed in case 1 produced amelioration rather than aggravation of the dermatosis.

In various papers in which results were dependent on interpretation of the reaction of the skin of animals to irritation we have seen no specific statement indicating that the investigators recognized the differences in the irritability of pigmented and nonpigmented skin. It is probable that this has not been a serious source of error as white animals are almost universally employed in irritation experiments because of the greater ease of reading reactions.

Correlation of the wide group of observations which were of interest to us in the cases under discussion is extremely difficult. It is interesting to note, however, that two light-sensitive dermatoses are markedly influenced by gold compounds. The first, lupus erythematosus, commonly responds by healing, while the second, psoriasis, apparently responds by an abnormal percentage of toxic reactions (Throne, Kingsbury and Myers), although the toxic reactions do not occur in the psoriatic lesions. It is difficult to state whether the reaction to gold compounds in our cases of vitiligo, another light-sensitive dermatosis, is in any way analogous, but the coincidence of these observations seems worthy of consideration.

SUMMARY

Two cases of vitiligo are described in which a dry papulosquamous dermatitis limited to the depigmented skin occurred following the use of gold sodium thiosulphate intravenously. In one case the presence of gold was demonstrated in the skin from the involved area by the method of Christeller. Microscopic sections in this case showed rather severe inflammatory changes and numerous minute hemorrhages limited strictly to the papillae and the subpapillary parts. Patch tests with gold sodium thiosulphate were negative, while the intradermal tests were slightly more marked in the depigmented skin, but the slight variance did not permit drawing any conclusions. However, it was concluded that the photosensitivity of the depigmented patches was not the controlling factor in the development of the gold dermatitis in our cases.

A review of the literature emphasizes the multiform character of reactions to gold compounds, the greater frequency of reactions dependent on the cumulative effect rather than true anaphylaxis and the fairly marked tendency of gold dermatitis to leave pigmentary remains which may be confined to the exposed surfaces. The available information on the histology of gold dermatitis is not large, and we were unable to correlate the reported findings closely with those observed in one of our cases. There would seem, however, to be a tendency to limitation of the pathologic changes to the region of the papillae in many cases.

Information indicating considerable physiologic variation in pigmented and nonpigmented skin in man and animals is available. Pigmented skin shows a greater reaction to various test substances than unpigmented skin. Infectious substances are reported to produce more marked inflammatory changes in pigmented skin in animals. Instances of various dermatoses tending to localize on pigmented as well as on unpigmented skin are reported. Pigmented skin likewise autolyzes with much greater rapidity than nonpigmented skin.

In accordance with the reported tendency of melanin to reduce gold salts, we believe that a logical theory of the peculiar localization of the gold dermatitis in our cases may be offered. The gold deposited in the depigmented skin might well fail to be reduced and eliminated, with the production of cumulative effects resulting in gold dermatitis.

LXII.—MENINGITIS AND DERMATITIS CAUSED BY A NEW VARIETY OF BLASTOMYCETE (ENDOMYCETE)

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AND
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Our purpose in this paper is to report the clinical record and autopsy observations in a fatal case of meningitis due to Endomyces capsulatus, occurring in a man, who had had a typical blastomycetic dermatitis for three years. The organism was recovered during life from the spinal fluid, blood and urine. A study and description of the morphology, cultural characteristics and animal pathogenicity of the organism are included. A review of the literature of systemic blastomycosis is presented, with special reference to involvement of the central nervous system.

Since Busse and Buschke [1] first described a case of generalized infection with a yeastlike organism, there have been about sixty reports of systemic infections, most of them under the term "blastomycosis." Gilchrist and Stokes [2] were the first to describe cutaneous blastomycosis, and there are now over two hundred cases of "blastomycetic dermatitis" in the literature. In only a few cases has a satisfactory study been made of the etiologic agent. The classification of the organism is, therefore, uncertain, and the generic names applied have created a chaotic medical literature. Most writers have been satisfied to call "blastomycosis" any disease which is caused by a doubly refractile yeastlike organism showing budding, but no mycelia in the tissues, but producing abundant mycelia in culture. Blastomycosis will probably be retained as a broad general term referring to infections of this type, but much can be learned by a more careful differentiation of the causative organism in each case, and in the future such study may yield information of considerable clinical value.

Studies, observations and reports from the medical and dermatological departments of the Barnard Free Skin and Cancer Hospital and the School of Medicine, Washington University, service of Dr. M. F. Engman and Dr. W. H. Mook, St. Louis.

1. Busse and Buschke, A.: Virchows Arch. f. path. Anat. **140**:23, 1895.

2. Gilchrist, C., and Stokes, J.: Bull. Johns Hopkins Hosp. **7**:1296 (July) 1896.

We believe the following case worthy of report, because of the infrequency of involvement of the central nervous system in systemic blastomycosis; because it is the first case described in which a true blastomycetic meningitis followed a blastomycetic dermatitis, and because it is the second case of meningitis reported as due to Endomyces capsulatus.

REPORT OF A CASE

History.—E. H., aged 28, an American born white man of Irish descent, had lived on a farm in Missouri until seven years before being seen by us. He had been working as a plumber at the time of the appearance of the skin lesions. The family history was essentially unimportant, as was the past history, except for pneumonia three times and otitis media in childhood.

About one year before his first entry to the hospital, there appeared a dime-sized lesion covered with a scab on the skin just to the right of the anus. Shortly afterward similar lesions appeared on the medial aspect of the upper part of the right arm and on the dorsal surface of the left wrist. After about two months the lesion on the right arm healed spontaneously, leaving a dark red, thin, smooth scar, while the two other lesions slowly increased in size. A physician diagnosed the condition as syphilis and administered antisyphilitic treatment for almost a year regardless of repeated negative Wassermann tests, but there was no improvement.

First Entry.—The patient was admitted to the Barnard Free Skin and Cancer Hospital on Feb. 24, 1930. There was on the left forearm, just above the wrist, a palm-sized annular ulceration, involving chiefly the dorsal surface and showing the characteristics of blastomycetic dermatitis. Smears of the pus obtained from the lesion showed round doubly-contoured budding forms. Just to the right of the anus was a similar lesion about 3 cm. in diameter, involving the anal margin. On the upper part of the right arm a thin, dark scar, about 3 cm. in diameter, marked the site of the lesion, which had spontaneously healed. All active lesions itched and had a foul odor. The physical examination otherwise gave negative results. The patient's general health did not seem impaired. Roentgen examination of the lungs was reported as essentially negative. Examination of the sputum failed to show blastomycetes.

During two and a half months in the hospital, the patient received inhalations of ethyl iodide and superficial roentgen therapy with considerable improvement. He was then discharged and followed in the clinic for two and one-half years. During this time he received saturated solution of potassium iodide, from 75 to 100 minims (4.62 to 6.16 cc.) daily by mouth, and a total of ten superficial roentgen treatments. At the end of six months the lesion on the arm was healed except for a small band of miliary abscesses at its lower border, and the rectal lesion was much smaller. The lesions then became worse, and gradually increased in size until the patient again came into the hospital.

Second Entry.—The patient was readmitted to the hospital on Dec. 8, 1931. The lesions were of the same warty character described at the first entry but were about one and one-half times as large. Other physical findings were negative. Roentgen examination of the lungs showed chronic hilar and peribronchial thickening within normal limits. Roentgen examination of the pelvis, left arm and vertebrae showed no pathologic lesions. Laboratory data on second entry were essentially normal, except for a moderate secondary anemia and positive smears for blastomycetes from the lesions.

Course in the Hospital.—The patient seemed to be in good general health on entry. From Dec. 8, 1931, to Jan. 12, 1932, he received 90 minims (5.58 cc.) of potassium iodide a day. On January 12 he complained of coryza, with a mild cough, and his temperature was 99 F. The following day he complained of pain in the right temporal region, and his temperature rose to 100 F. During the next few days the pain became more intense, and on January 21 he had a universal headache, quite intense and deep, posterior to the eyes and extending to the occiput and base of the neck. He became somewhat nauseated and vomited several times,

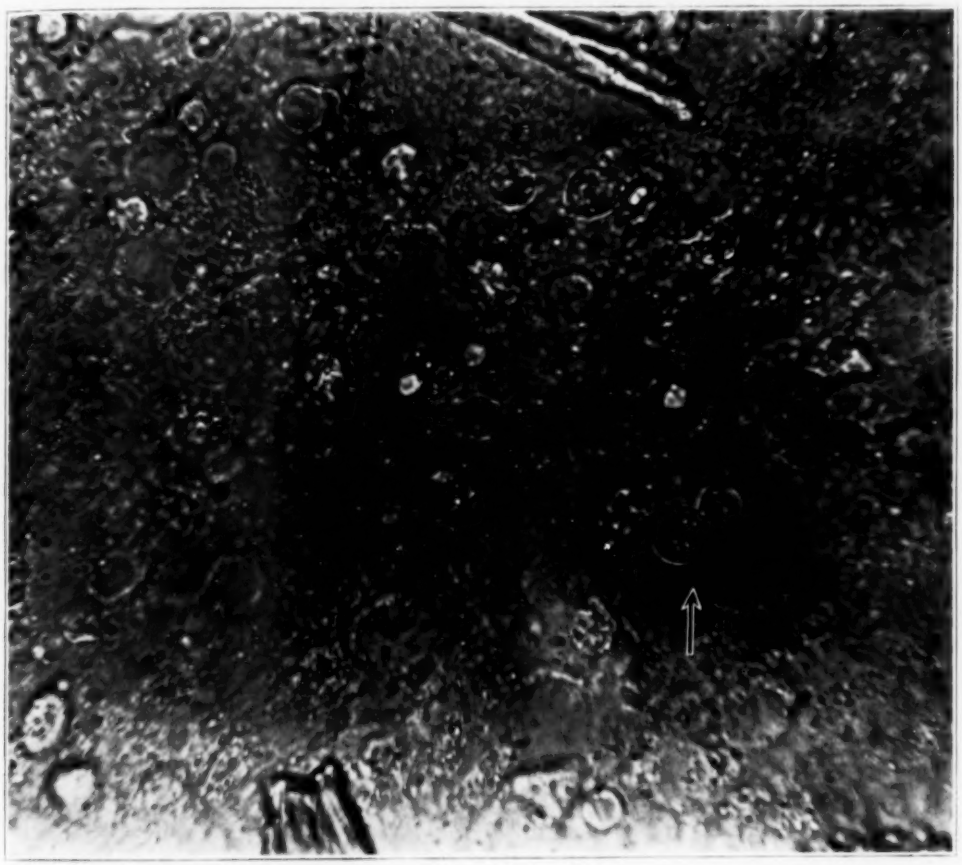

Fig. 1.—Hanging drop preparation from centrifugated sediment of spinal fluid; × 1,000. Note the budding blastomycete.

and his temperature rose to 101.5 F. The eyegrounds were normal. The general physical and neurologic examination gave negative results except for markedly hyperactive reflexes, stiffness of the neck and a bilaterally positive Kernig's sign. The white count was 4,200, and the differential count showed no eosinophils, 8 stab forms, 30 segmented forms, 56 lymphocytes and 6 mononuclears.

Lumbar puncture on January 21 yielded cloudy fluid under slightly increased pressure. There were 452 cells per cubic millimeter, of which 58 per cent were

neutrophils. In the counting chamber were seen many doubly contoured rounded forms somewhat larger than the white cells. A few of them were budding. The Pandy test was three plus, and a cobweb-like pellicle formed through the center of the tube on standing. Smears for tubercle bacilli and other bacteria were negative. Subsequent lumbar punctures and cisterna magna punctures were done, showing an increasing number of cells and blastomycetes (fig. 1).

The accompanying table shows the results of six different examinations of the cerebrospinal fluid during blastomycetic meningitis; the fluid for the first three examinations was obtained by lumbar puncture and for the last three by cisterna magna puncture.

The blastomycetes were found in the urinary sediment and were easily cultured from the urinary sediment, spinal fluid and from the blood. The growth at incubator temperature was chiefly by budding, and at room temperature chiefly by profuse mycelial formation (fig. 2). The character of the organism will be discussed more fully. It was classified as Endomyces capsulatus-isabellina (new variety).

Examinations of Cerebrospinal Fluid

Date	Pressure	Color	White Blood Cells per Cu. Mm.	Differential Cell Count, per Cent: Segments	Differential Cell Count, per Cent: Lymphocytes	Blastomycetes per Cu. Mm.	Pandy Reaction	Additional Data
1/21/32	Slightly increased	Cloudy	452	58	42	Many	+++	Wassermann, negative; dextrose, 53 mg. per 100 cc.; protein, 100 mg. per 100 cc.
1/22/32	Normal	Cloudy	650	56	44	Many	+++	
1/23/32	Normal	Cloudy	700	38	62	600	+++	
1/24/32	Normal	Turbid	1,150	61	39	1,100	+++	Wassermann negative
2/ 5/32	Normal	Much clearer	120	33	67	25	++	Iodide, 175 mg. per 100 cc. (normal iodide = 0.018 mg. per 100 cc.)
2/17/32	Normal	Clear	63	0	100	Very few	+++	Colloidal gold, 55555555553

The patient continued to complain of severe headache, and stiffness of the neck, and the bilateral Kernig's sign became more marked during the next few days. The temperature ranged from 100 to 101 F. On January 28, the patient was given 0.5 Gm. of sodium iodide in 10 per cent solution intravenously. Thereafter he was given increasing daily doses of sodium iodide and an alcoholic solution of iodine and hydriodic acid especially prepared for intravenous administration, until on February 5 he received 60 cc. of combined iodine solution intravenously in a 5 per cent solution of dextrose. This was equivalent to 3 Gm. of iodine and 6 Gm. of sodium iodide. As it seemed important to determine how much of this enormous dose of iodine reached the spinal fluid, a cisterna magna puncture was done one and one-half hours later. Iodine (as iodide) was present in amounts of 175 mg. per hundred cubic centimeters of spinal fluid, which is approximately 9,722 times the normal [3] amount. The fluid was no longer cloudy, as it had been eleven days before, and the cell count had fallen from 1,150 to 120. Blastomycetes were present, but were rare.

3. Osborne, E. D.: Iodin in the Cerebrospinal Fluid, with Special Reference to Iodid Therapy, J. A. M. A. **76**:1384 (May 21) 1921.

Catton [4] concluded that regardless of the amount of iodine administered by mouth, none could be found in the spinal fluid. Publications [3] previous to 1921 stated that iodides do not appear in the spinal fluid.

The patient experienced a marked toxic reaction for several days following the last intravenous injection of iodine. He was given a transfusion of 500 cc. of citrated blood. Following the transfusion he became clear mentally, and the pulse and temperature returned to normal. He said that he felt much better. During the next two weeks the patient received three transfusions followed by temporary

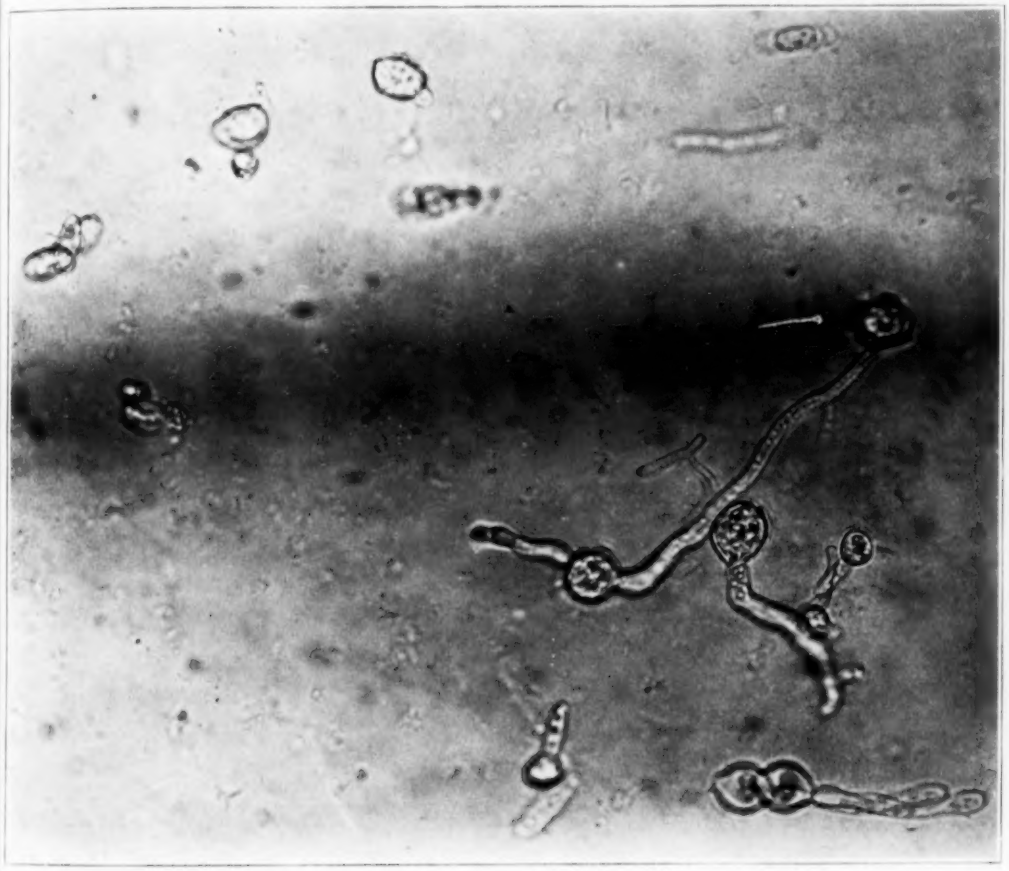

Fig. 2.—Smear from culture from spinal fluid obtained at first lumbar puncture. The culture was two weeks old and grown at room temperature on Sabouraud's medium; × 1,000.

general improvement. He then had a relapse and became drowsy and irrational. Three days before death three small subcutaneous abscesses appeared, one on the right wrist, one on the sacrum and one on the left side of the chest; all contained pus, which yielded blastomycetes on culture. The patient became comatose and died

4. Catton, J. H.: Studies of Spinal Fluid During Iodid Medication by Mouth, J. A. M. A. **67**:1369 (Nov. 4) 1916.

forty-six days after the onset of meningitic symptoms and about three years after the first appearance of the skin lesions.

The clinical diagnoses were blastomycetic meningitis and blastomycetic dermatitis.

Autopsy.—An autopsy, performed ten hours post mortem by Dr. L. H. Jorstad, was negative except for the changes in the brain and skin. Dr. Jorstad's report follows:

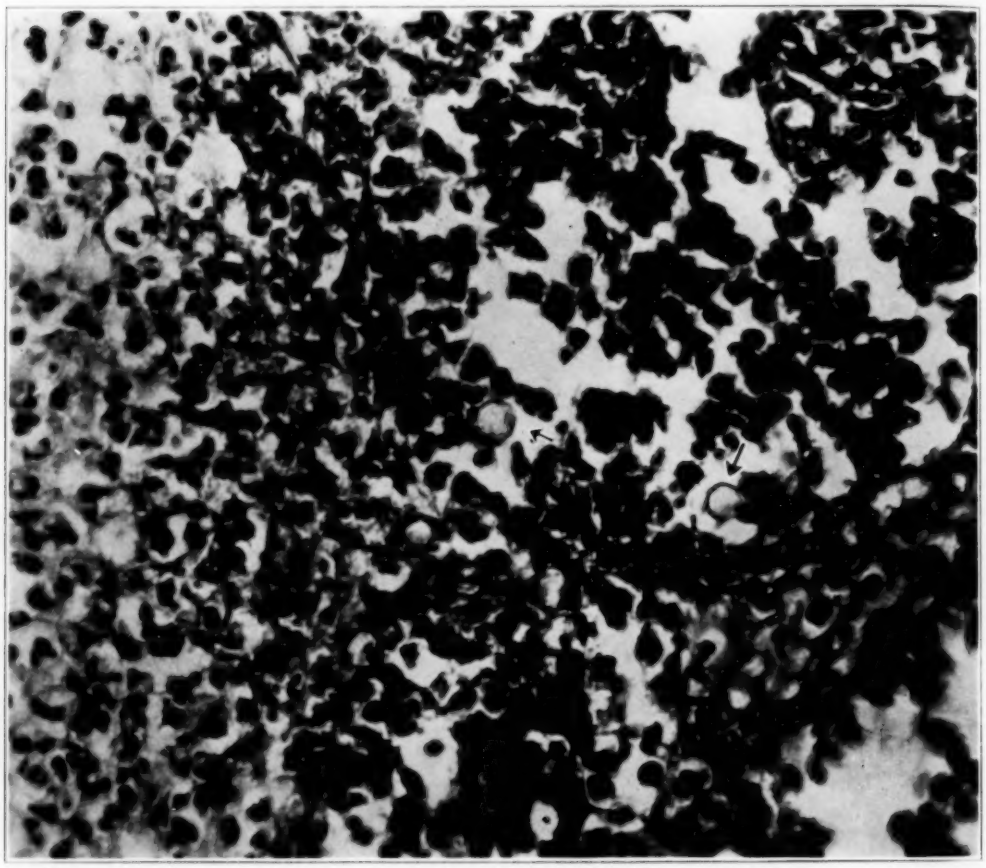

Fig. 3.—Microscopic section of meninges showing several encapsulated forms; × 1,000.

A section of the spinal cord removed through the thorax appeared normal.

The scalp and calvarium were normal.

On removing the brain, there was noted some exudate around the foramen ovale. The brain presented a moderate amount of tenacious, partially organized exudate on the ventral surface of the cerebellum posterior to the pyramids. Over the ventral surfaces of the cerebri were numerous pinpoint, translucent papules. On section, the brain was quite normal, excepting for the presence of 3 cc. of thick, grayish-white exudate in the left lateral ventricle. After removal of the

exudate, the entire surface of the ventricle presented a rough translucent appearance in contrast to the normal shiny smooth surface of the right ventricle.

The gastro-intestinal tract, kidneys, ureters, bladder, prostate and heart showed no gross pathologic lesions.

The anatomic diagnosis was: blastomycetic dermatitis; basilar meningitis, possibly mycotic; acute splenitis; fibrous, adhesive pleurisy, and cutaneous abscesses.

Microscopic Examination.—The significant microscopic changes were as follows: The surface of the skin was ulcerated; the epithelium at the edge of the ulcer showed acanthosis and hyperplasia. The bed of the ulcer was made up of polymorphonuclear leukocytes, lymphocytes, a few plasma cells and giant cells. In the deeper tissues and in the subcutaneous tissue, some distance away from the ulcer proper, were small abscesses. Scattered throughout the skin section were rounded, encapsulated organisms, somewhat larger than the leukocytes, some of them budding.

The convoluted and straight tubular portions of the kidney showed marked destruction. There was a moderate amount of hemorrhagic exudate in the glomeruli.

There were scattered areas of acute bronchopneumonia in the lungs, and at one point there was a definite small abscess, the center of which was entirely necrotic. The periphery was made up of inflammatory cells, with an occasional encapsulated budding organism.

There was a moderate amount of polymorphonuclear leukocytic exudate surrounding the spinal cord and on the meninges.

The exudate on the ventricular wall of the brain was made up of polymorphonuclear leukocytes, fibrin, lymphocytes, plasma cells and an occasional giant cell. Blastomycetes appeared throughout, especially in or near the giant cells.

The microscopic diagnosis was: blastomycetic dermatitis, blastomycetic meningitis and pulmonary blastomycosis (fig. 3).

Culture.—The organism was cultured from the skin lesions and from the exudate on the meninges. The morphologic and cultural characteristics were the same as those obtained in the study of the growth from the spinal fluid obtained during life.

SYSTEMIC BLASTOMYCOSIS

Blastomycosis occurs in man in two forms, cutaneous and systemic. However, the systemic form rarely develops from the cutaneous type, the atrium of infection in nearly all the systemic cases being, apparently, the lungs. Stober,[5] in a review of twenty-eight cases of the systemic form, found only three following the cutaneous disease.

Cutaneous blastomycosis develops usually in healthy young men, aged from 30 to 35, employed at normal labor. The fully developed lesions resemble the verrucous type of lupus vulgaris. They appear first as papules or nodules, which spread gradually over a period of months or years until raised, warty patches several inches in diameter, with a border of miliary abscesses, are formed. The lesions are usually multiple, the commonest sites being the face (50 per cent), the hands (12 per cent) and the feet (8 per cent), although any part of the

5. Stober, A. M.: Systemic Blastomycosis: A Report of Pathological, Bacteriological and Clinical Features, Arch. Int. Med. **13**:509 (April) 1914.

surface of the body may be involved. The disease is very refractory to treatment, roentgen therapy, iodides and excision being sometimes followed by disappearance of local lesions, but recurrence is the rule. In most of the cases the condition remains local, and there is no disturbance of the general health or enlargement of the neighboring lymph glands.

Montgomery and Ormsby,[6] Stober,[5] Wilhelmj,[7] Michelson,[8] and D'Aunoy and Beven[9] have each analyzed a series of systemic case reports and summarized the chief clinical features and pathologic changes.

The generalized infection, beginning most commonly in the lungs, is ordinarily confused with pulmonary tuberculosis at the start, as there are cough, hemoptysis, loss of weight, low grade fever and night sweats. There is occasionally hoarseness from involvement of the larynx. As a rule, the pulmonary symptoms are much less marked than those that occur in tuberculosis with an equal amount of involvement of the lungs. A number of systemic cases have first been manifested by the appearance of subcutaneous abscesses. It is probable that the lungs are the primary focus in these cases also, since 90 per cent of all cases show pulmonary involvement at autopsy, and since those cases beginning with definite pulmonary signs practically always develop multiple subcutaneous abscesses later. Pathologically as well as clinically, there is difficulty in distinguishing blastomycosis and tuberculosis. Coincident infection by the tubercle bacillus and blastomycetes has been reported by F. H. Montgomery,[10] Vinson, Broders and Montgomery,[11] and Rewbridge, Dodge and Ayers.[12]

Following the development of pulmonary symptoms and subcutaneous abscesses, there is cough with blood-flecked or purulent sputum, the abscesses may break down and form sinuses or ulcers draining purulent material, and there is fever, from 101 to 103 F., with increasing loss of strength and emaciation. Any organ or structure of the body may be involved. Enlargement of the spleen and

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6. Montgomery, F. H., and Ormsby, O. S.: Systemic Blastomycosis; Its Etiologic, Pathologic and Clinical Features as Established by a Clinical Survey of Twenty-Two Cases, Arch. Int. Med. **2**:1 (Aug.) 1908.

7. Wilhelmj, C. M.: Am. J. M. Sc. **169**:712 (May) 1925.

8. Michelson, I. D.: Blastomycosis: A Pathologic and Bacteriologic Study, J. A. M. A. **91**:1871 (Dec. 16) 1928.

9. D'Aunoy, R., and Beven, J. L.: J. Lab. & Clin. Med. **16**:124 (Nov.) 1930.

10. Montgomery, F. H.: J. Cutan. Dis. **21**:19 (Jan.) 1903.

11. Vinson, P. P.; Broders, A. C., and Montgomery, H.: Surg., Gynec. & Obst. **42**:255 (Feb.) 1928.

12. Rewbridge, A. G.; Dodge, C. W., and Ayers, T. T.: Am. J. Path. **5**:349 (July) 1929.

liver, progressive anemia, moderate leukocytosis and involvement of the bones or joints are frequent. The sputum and the pus from the abscesses may reveal the organism. In some cases the organism has been found in the urine and in a few cases cultured from the blood. Death results from exhaustion due to the chronic pyemia or from involvement of vital structures. The prognosis is about 90 per cent fatal. Systemic blastomycosis may be simulated by pyoderma, bromoderma, iododerma, glanders, sporotrichosis, scrofuloderma and ulcers of glandular tularemia.

In a clinical study of twenty-seven cases by Montgomery and Ormsby (twenty-two proved and five probable), pulmonary involvement was present in practically every case. Anemia, laryngitis and hemoptysis were present in 20 per cent of these cases, while the following organs, liver, spleen, eye, lymph glands, bones and joints, were involved in order from 7 to 40 per cent. Blastomycetes were found in the sputum in six cases, in the urine in one case and by culture from the blood in two cases. Eighty-five per cent of the cases were in men, the average age being 32; 60 per cent began with skin and subcutaneous involvement, and only one patient recovered.

Wilhelmj,[7] in 1925, was able to collect reports of thirty-three systemic cases with autopsies. Of these, twenty began with signs of pulmonary involvement. Seven began with cutaneous lesions, four had abscesses and three had blastomycetic dermatitis. Of the remaining six, three began with vague symptoms in the joints, one with abdominal pain and ascites and one with infection of a tooth socket, and in one the primary symptoms were not stated.

Combining the eleven autopsy reports of Montgomery and Ormsby and the thirty-three of Wilhelmj, we find that the lungs were involved in 91 per cent of the forty-four cases, the spleen in 82 per cent, the skin and subcutaneous tissues in 76 per cent, bones and joints in 72 per cent, and the kidneys in 62 per cent. Other organs, including practically every tissue and system, were less frequently involved. The brain was involved in 27 per cent and the meninges in 12 per cent of the cases.

BLASTOMYCOSIS OF THE CENTRAL NERVOUS SYSTEM

Involvement of the brain and meninges is one of the least frequent complications of systemic blastomycosis. This is evident from the clinical reports of cases and is borne out by the analysis of the distribution of lesions found at autopsy. The central nervous system is usually involved either by direct extension through the skull or vertebrae, or as a part of the terminal pyemia, with the formation of one or more brain abscesses.

Stoddard and Cutler [13] pointed out the distinguishing characteristics between torulosis and those infections classified as blastomycosis. Torula has a predilection for, and is typically a chronic disease of, the nervous system, without fever or leukocytosis. Systemic involvement may occur, but the skin and bones are not involved. The symptoms are usually like those of brain tumor with papilledema, headache, vomiting and mental symptoms, sometimes hemiplegia or cerebellar signs. At autopsy, gelatinous cysts are found in the brain and meninges; cellular reaction is slight, and there is little or no pus in the lesions.

Blastomycosis, on the contrary, is typically a chronic skin disease or a pulmonary infection. There is infrequently systemic involvement, and when it does occur, the central nervous system is rarely involved. Systemic blastomycosis, unlike torula, is characterized by the formation of multiple abscesses, accompanied by considerable cellular reaction with pus formation and fever. Basilar meningitis or brain abscesses are found at autopsy. There is no gelatinous exudate or cyst formation.

Rewbridge, Dodge and Ayers,[12] in 1929, collected eighteen reports of cases of meningitis in which Torula histolytica was the etiologic factor.

Ryfkogel,[14] in 1910, reported a case of coccidioidal meningitis. Others have reported brain abscesses due to Coccidioides.

A case of sporotrichosis meningitis was reported in 1926 by Hyslop, Neal, Kraus and Hillman.[15]

Meningo-encephalitis due to Trichomyces occurring in a case of pulmonary tuberculosis was reported in 1925 by Vialard, Lancelin and Darleguy.[16]

In 1925, Wilhelmj [7] collected reports of four cases of blastomycetic meningitis of the secondary type, described by Riley and LeCount,[17] McKenty and Morgan,[18] Hurley [19] and Moore.[20] These cases corre-

13. Stoddard, J. L., and Cutler, E. C.: Monograph of the Rockefeller Institute for Medical Research, 1916, no. 6.

14. Ryfkogel, H. A. L.: Coccidioidal Meningitis, with Secondary Internal Hydrocephalus and Death (Anaphylactic?) Following a Second Injection of Flexner's Serum, J. A. M. A. **55**:1730 (Nov. 12) 1910.

15. Hyslop, G. H.; Neal, J. B.; Kraus, W. M., and Hillman, O.: Am. J. M. Sc. **172**:726 (Nov.) 1926.

16. Vialard, Lancelin and Darleguy: Bull. et mém. Soc. méd. d. hôp. de Paris **48**:1284 (July 25) 1924.

17. Riley, F. B., and LeCount, E. R.: A Case of Systemic Blastomycosis, Arch. Int. Med. **13**:614 (April) 1914.

18. McKenty, F. E., and Morgan, D.: Ann. Surg. **41**:513 (May) 1915.

19. Hurley, T. D.: J. M. Research **33**:499 (Jan.) 1916.

20. Moore, J. T.: Surg., Gynec. & Obst. **31**:590 (Dec.) 1920.

spond to the foregoing description of systemic blastomycosis with secondary involvement of the central nervous system. Riley and LeCount's case began with pulmonary symptoms, as did the one reported by Hurley. McKenty and Morgan's case began with a nodule near the eye followed by penetration through the skull. Moore's case began with infection in a tooth socket, followed by necrosis of bone and penetration of the skull. In none of them was there a blastomycetic dermatitis.

Two similar cases have been reported by Farnell and Starr [21] and Montgomery.[22] Montgomery's case began with a nodular swelling of the wall of the chest. In Farnell and Starr's case, the organism was cultured from the spinal fluid, and there was a severe meningitis, from which the patient recovered. He was alive six months later, but there were subcutaneous abscesses present from which the blastomycetes could be obtained.

In addition to the four secondary cases presented by Wilhelmj, he cites five others as primary blastomycetic meningitis. These are the cases of Rusk and Farnell,[23] Turck,[24] von Hausemann,[25] Goto,[26] and Swift and Bull.[27] By clinical course, autopsy findings and cultural studies, the first four should probably be classed as due to Torula. They are so classified by Greenfield [28] on the basis of Stoddard and Cutler's criteria.

Swift and Bull's case was called a saccharomycetic infection by the writers. There was attempted mycelial formation in the first culture; no mycelia formed in subcultures. This case occurred in a 53 year old Chinaman, who had complained of headache and failing vision for five weeks. No cutaneous lesions or pulmonary symptoms were present. The spinal fluid was turbid and under considerable pressure, and the organism was cultured from the fluid. Autopsy showed a diffuse cerebrospinal meningitis and an acute myelitis of the dorsal cord.

Wilhelmj added a case report of his own to the first five classed in the primary group. Meningitis resembling that of tuberculosis was found at autopsy, with budding organisms present in the meninges. No cultures were made.

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21. Farnell, F. J., and Starr, Samuel: Boston M. & S. J. **176**:771 (May 31) 1917.
22. Montgomery, H.: M. Clin. North America **14**:651 (Nov.) 1930.
23. Rusk, G. Y., and Farnell, F. J.: Univ. California Publ., Pathology **2**:47, 1912.
24. Turck: Deutsches Arch. f. klin. Med. **90**:367, 1907.
25. von Hausemann: Centralbl. f. allg. Path. u. path. Anat. **16**:802, 1905.
26. Goto, K.: Mitt. a. d. med. Fakult. d. k. Univ. zu Tokyo **15**:75, 1915.
27. Swift, H., and Bull, L. B.: M. J. Australia **2**:265, 1917.
28. Greenfield, J. G.: M. Science **10**:267 (July) 1924.

Gáspár [29] reported a case in 1929 which he diagnosed as primary meningeal blastomycosis, and which he added to the foregoing series of six. The patient had symptoms of brain tumor. There was no generalized involvement, no fever or leukocytosis. Craniotomy was performed, and a large granulomatous tumor adherent to the dura was removed. There was no cultural study. The case probably was one of torula infection.

In addition to the one reported by Swift and Bull, three other cases of primary meningitis have been reported from Australia by Williams,[30] Badham,[31] and Barlow.[32] In Williams' case there were headache and failing eyesight for five months before death. At autopsy there were purulent meningitis and consolidation of one lung. The organism was cultured and classified as Saccharomyces. Badham cultured the organism from his case and found it to form ascospores and aerial hyphae in culture. He called it Saccharomyces. In Barlow's case there was death four months after the onset of meningeal signs. No cultural study was reported, but a dog given intrathecal injection with the spinal fluid died of meningitis, a budding organism being found in the meninges.

The four Australian cases differ radically in clinical and autopsy findings from the reports of cases of meningitis due to Torula histolytica. They have been accepted as being due to saccharomycetic infection. The classification of the case reported by Wilhelmj is uncertain.

In 1929, Rewbridge, Dodge and Ayers [12] reported the first case of meningitis due to Endomyces. This occurred in a 48 year old man, the first symptom being a tender swelling on the thigh. Later, other subcutaneous abscesses developed, from which creamy yellow pus was aspirated. Headaches and loss of memory developed gradually; there was confusion, and the patient came into the hospital five months after the onset. There were positive physical signs of meningitis. Lumbar puncture disclosed that the cell count was 20, of which 15 were polymorphonuclears. The organisms were not seen in, or cultured from, the spinal fluid. The patient, after increasing signs of meningeal involvement, died two months after entering the hospital. At autopsy the lower surface of the brain and brain stem was covered with numerous small nodules, not involving the brain substance. The organism was demonstrable, microscopically, in these nodules.

A complete study of the morphologic and cultural characteristics of the organism was made, and it was identified as Endomyces capsu-

29. Gáspár, István: Blastomycotic Meningo-Encephalitis, Arch. Neurol. & Psychiat. **22**:475 (Sept.) 1929.

30. Williams, J. R.: M. J. Australia **2**:185, 1922.

31. Badham, C.: M. J. Australia **2**:385, 1922.

32. Barlow, D. L.: M. J. Australia **2**:302, 1923.

latus (new species). The organism was found to be pathogenic for mice, but not for rabbits or guinea-pigs.

The case we report in this paper is the second case to be recorded of systemic infection in man due to Endomyces. It is the second case of meningitis reported as due to Endomyces capsulatus, and we believe it is the first case reported of meningitis following a typical blastomycetic dermatitis.

A culture from the first lumbar puncture, on Sabouraud's dextrose agar was furnished to Morris Moore, of the cryptogamic laboratory, Henry Shaw School of Botany, Washington University, who made a complete study of the morphologic and cultural characteristics of the organism. He identified it as a new variety of Endomyces capsulatus, described as the causative organism in the case of Rewbridge, Dodge and Ayers.[12]

Prof. Carroll W. Dodge of the Henry Shaw School of Botany aided in the classification and confirmed the identification of the organism.

Mr. Moore's report of the study of the organism follows:

ENDOMYCES CAPSULATUS REWBRIDGE, DODGE AND AYERS, VARIETY ISABELLINUS MOORE, NEW VARIETY[33]

In lesions and when first isolated, the mycelium of the fungus consists of thick-walled, yeastlike, budding cells, from 3.5 to 5.5 microns in diameter, varying in the mediums, with the substrate and with the hydrogen ion concentration (fig. 4, *1* to *8*). In the tissue, the cells secrete thick, clear, nonstaining capsules about themselves, the nature of which is as yet unknown (fig. 4, *6* and *7*). In broth cultures and on agar mediums, when first isolated, the organism grows in chains of thin-walled, coarse, slightly elongated, symmetrical cells with an abundance of budding, corresponding to the oidia of Brumpt (fig. 4, *21* and *31*). These cells measure from 3.5 to 7.5 microns.

Continued transfers on artificial mediums and growth on acid substrates cause the yeast cells to bud mycelial strands, and a filamentous culture rapidly replaces the oidia-like cells (fig. 4, *9* to *13*). The hyphae thus formed vary in thickness with the hydrogen ion concentration and the nutrient materials present, being long and thin, from 1.2 to 1.5 microns wide, on acid mediums, and varying from 2.2 to 3 microns on neutral or alkaline substrates.

Mediums with protein as the source of nitrogen, and a good carbohydrate, usually glycerin, present the best growth for study. The hyphae are branched, with cross-walls, having swollen portions, from

33. Varietas isabellinus Moore, var. nov.; colore cinnamomeo-alutaceo vel dilute isabellina, ab specie differt.

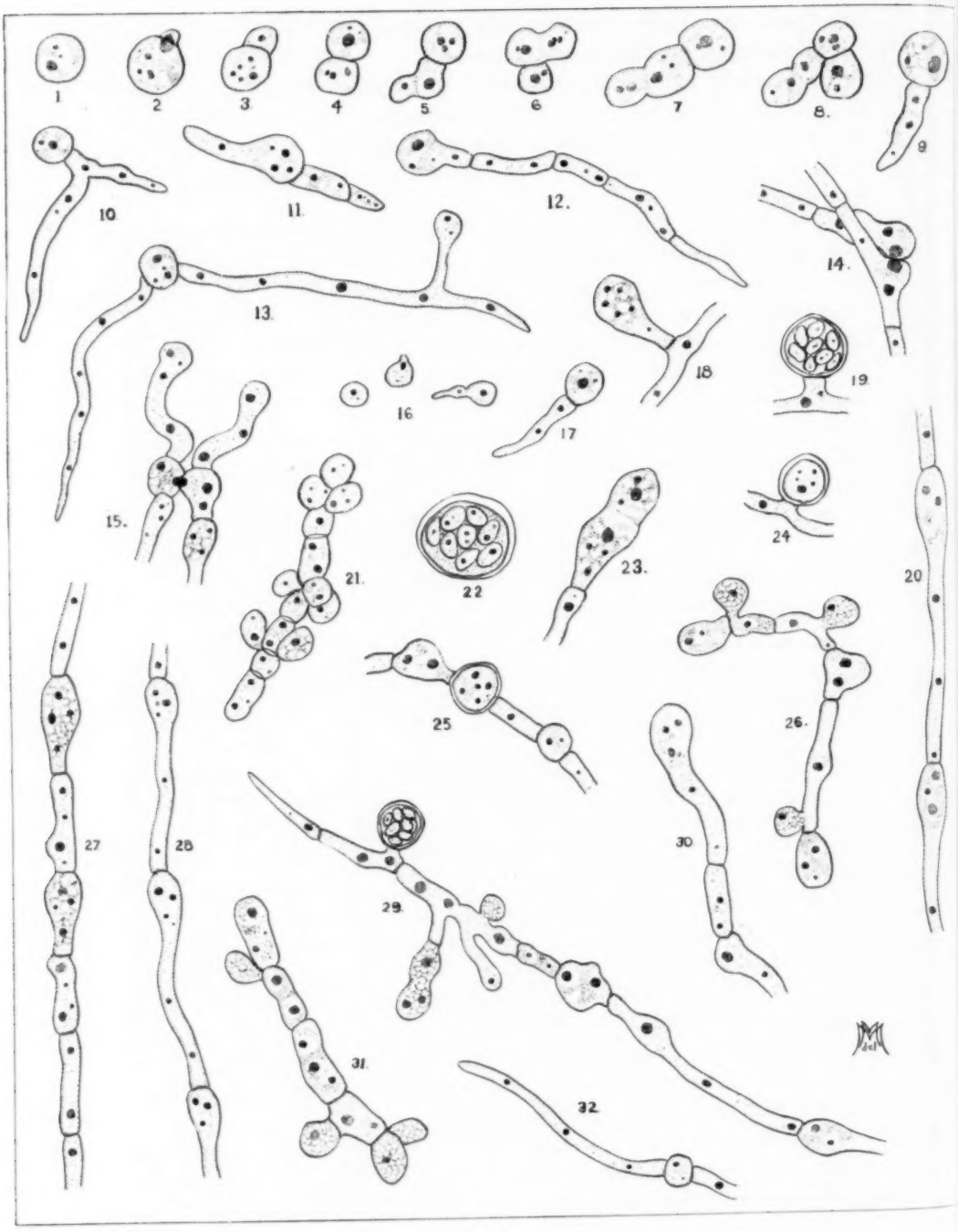
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Fig. 4

EXPLANATION OF FIGURE 4

All of these drawings were made by camera lucida and reproduced as correctly as possible. The interpretation of several of the figures rests on cytologic work being carried on at the present time in the original species. The magnification is × 1,440. *1, 2, 3, 4, 5, 6, 7* and *8:* yeastlike cells in original culture showing budding forms in *2, 3* and *4*. The culture was isolated on Sabouraud's dextrose agar and then transferred to 2 per cent aqueous bacto-peptone. *9, 10* and *11:* saccharomycetous cells developing mycelium in a hanging-drop culture of 2 per cent aqueous solution of bacto-peptone plus 5 per cent meat extract. *12* and *13:* later stages in *9, 10* and *11*. *14:* heterogamous copulation, premature stage, on Sabouraud's agar. *15:* heterogamous copulation at time of transfer of nuclear material, seen in hanging-drop of 2 per cent aqueous proteose peptone plus glycerin. *16:* germinating spore on glycerin agar. *17:* germinating spore developing hypha on lactose broth. *18:* developing ascus on Sabouraud's agar. *19:* ascus showing eight spores on nutrient agar. *20:* racquet mycelium on lactose agar. *21:* oidia-like cells formed in Sabouraud's broth. *22:* mature ascus showing eight spores, potato dextrose agar. *23:* terminal hypnospore (chlamydospore), on glycerin agar. *24:* large round chlamydospore with a thick wall, in cornmeal agar. *25:* section of a mycelium showing a thick-walled chlamydospore in a hanging-drop of 2 per cent bacto-peptone (aqueous). *26:* mycelium with conidia on glycerin agar. *27:* mycelium on eosin-methylene-agar. *28:* racquet mycelium on Sabouraud's agar. *29:* mycelium showing racquet formation, conidia, hypnospores and an eight-spored ascus, on glycerin agar. *30:* terminal hypnospore on 2 per cent proteose peptone plus glycerin. *31:* monilia-like growth in nutrient broth. *32:* young hypha, 2 per cent bacto-peptone hanging-drop culture.

3.5 to 5 microns, by 6 microns, resembling the racquet mycelium of Trichophyton and simulating somewhat that present in Coccidioides immitis. These enlarged regions develop into chlamydospores.

Hypnospores (chlamydospores), either terminal on hyphae or on short branches, approximately 5 by 11 microns (fig. 4, *23, 24, 29* and *30*), are characteristic. Conidia, developing on the hyphae, usually near a cross-wall (fig. 4, *26*), are abundant, being piriform and sessile and measuring 5 by 6 microns.

Copulations show that the sexual reproduction, so far, is present and heterogamous. Two cells, usually of unequal size, one thin and small (4.5 by 5.5 microns), but varying in size, and the other thick and large (5.5 by 11.5 microns), fuse to form an ascus. Further details are still under observation and study. The asci may be terminal on a filament or on a short branch on a hypha (fig. 4, *18, 19, 22* and *29*), varying in size from 5.5 to 12 microns in diameter and containing eight well defined spores.

Further descriptions are given in the cultural characteristics.

Cultural Characteristics.—All cultures were grown at 25 C. The original culture furnished in the case was growing on Sabouraud's dextrose agar. Having the characteristic yeastlike appearance, it was deemed advisable to transfer it to a series of mediums, both broth and agar, to determine whether any pleomorphism, which is being noted more and more with fungi of this sort, might occur. Having the general appearances which were so evident in the early isolation stages of the first organism, E. capsulatus, it was assumed that the fungus in question might in some way be related. As a result of observed physiologic phenomena, in this regard, mediums containing protein were used to a great extent. However, bearing in mind that Monilia or some other imperfect yeast was probable, acid mediums, on which these organisms grow well, were also used.

As will be seen from the cultural characteristics, the first assumption proved correct and nutrient mediums, with beef extract, were the most nutritional for the fungus.

The following mediums and descriptions are arranged in the order of decreasing hydrogen ion concentrations.

Czapek's Agar Modification by Dox (p_H 4.15): No growth at end of eleven days.

Malt Extract Broth (1.5 per cent malt extract, p_H 4.9): Very little growth at the end of nineteen days; few filaments, from 0.8 to 1 microns wide.

Malt Extract Agar (same as broth, plus 2 per cent agar, p_H 5.2): Growth poor; colony, 0.7 microns in diameter at end of eleven days, due no doubt to the hydrogen ion concentration; few hypnospores; round chlamydospores, 4 microns in diameter, or asci; cells thin-walled.

Sabouraud's Broth (Sabouraud's dextrose agar minus the agar, p_H 5.4): Growth at first in pinhead, yeastlike colonies, with an abundance of saccharo-

mycetous-like cells. With age, however, there is a change to oidia-like cells in chains which change to filamentous growth resulting in cottony clumps in the broth. Morphologically, the structures resemble those on meat extract broth.

Sabouraud's Agar (bacto-peptone and dextrose plus agar, p_H 5.6): Growth rapid, reaching a diameter of 4.4 cm. in nineteen days. It is of importance to note that when first isolated and transferred to Sabouraud's agar, the colony was moist, yeastlike and had lines radiating from the center of the colony. With age, or with several transfers, the culture assumed the cottony growth characteristic of the species on agar mediums. This is due, no doubt, to the adaptation of the fungus to its new source of nutrition and mode of life. Morphologically, the growth is similar to that on nutrient mediums, with an abundance of asci and racquet mycelium. Culturally, the color is chamois-like or light isabella, and the mycelium is abundant.

Oatmeal Agar (decoction of oatmeal, dextrin and agar, p_H 5.8): Growth sparse; filaments, thin and long.

Potato Dextrose Broth (decoction of potatoes and dextrin, p_H 5.8): Growth abundant; colonies in clumps of yeastlike cells in chains, becoming filamentous with age, from 4 to 6 microns in width; round cells; chlamydospores, 6 microns in diameter; hyphae, from 1.5 to 2 microns in width, being long; few asci or hypnospores; racquet mycelium not evident.

Potato Dextrose Agar (the same as the preceding plus agar, p_H 5.9): Growth slow; colony spinescent at first, then cottony; diameter of colony 1.4 cm., at end of nineteen days; mycelium abundant at inoculum; morphologic characteristics similar to those on Sabouraud's agar.

Cornmeal Agar (decoction of cornmeal plus dextrin and agar, p_H 6): Colony loose and cottony; growth slow, having a diameter of 0.8 cm. at end of eleven days, followed by the spread of long, thin hyphae over surface of agar; abundance of thick-walled, granular chlamydospores, arising on short stalks from a long filament.

Two Per Cent Aqueous Bacto-Peptone Plus 5 Per Cent Meat Extract (hanging-drop culture, p_H 6.2): Growth profuse, covering the drop in four days; hyphae from 2 to 2.5 microns wide, with an abundance of racquet mycelium, intertwining and branching; thick-walled cells; chlamydospores in abundance, as well as asci, 10 microns in diameter.

Two Per Cent Aqueous Bacto-Peptone (hanging-drop culture, p_H 6.2): Mass of hyphae thick-walled, ramifying and branching, from 2 to 2.5 microns wide; racquet mycelium not evident; numerous chlamydospores, 4 microns in diameter, and asci, from 4 to 6 microns; few terminal hypnospores, from 3.5 to 6 microns.

Two Per Cent Aqueous Proteose Peptone Plus 6 Per Cent Glycerin (hanging-drop culture, p_H 6.2): Growth similar to that on bacto-peptone broth, but with an abundance of chlamydospores and racquet mycelium.

Lactose Broth (2 per cent aqueous solution, p_H 6.8): Growth rapid; mycelium abundant; hyphae, from 3 to 3.5 microns wide, with coarse, thick-walled, numerous swellings and characteristic racquet mycelium; many chlamydospores, from 6 to 8 microns in diameter; several asci, approximately 12 microns in diameter.

Lactose Agar (p_H 6.8): Rapid growth; colony crateriform and fluffy, reaching a diameter of 1.7 cm. in eleven days; culture assumed the typical chamois-like or light isabella color after the sixth day; many hypnospores, 6 by 10 microns, and numerous eight-spored asci.

Meat Extract Broth (nutrient medium, p_H 6.8): Growth at first yeastlike, then formed profuse cottony clumps; chains of oidia-like cells, from 4 to 5 microns in diameter, simulating that of filamentous Moniliae; cells, from 3.5 to 5 microns wide, and approximately 12 microns long.

Eosin-Methylene-Blue Agar (medium used merely as a matter of curiosity to observe whether the results here obtained would be compatible with those occurring on the same substrate with the original species, p_H 7).: Growth slow, attaining a diameter of 0.7 cm. in eleven days; stain of medium absorbed by colony giving it a pink color; morphology similar to that on Sabouraud's agar.

Glycerin Agar (nutrient agar plus 6 per cent glycerin, p_H 7.1): Colony crateriform, with lines radiating from center of inoculum; culture moist and slimy on edge with heavy cottony center; growth 2.5 cm. in diameter in nineteen days with creamy color at first, turning to characteristic color later; asci, chlamydospores and swellings, numerous and similar to those on lactose agar.

Nutrient Agar (p_H 7.2): Growth rapid, diameter 4.8 cm. in nineteen days; colony slightly crateriform; heavy, matted growth at inoculum surrounded by a loose, smooth, feltlike mycelium; isabella color; hyphae, 2.5 microns in width, with eight-spored asci, from 9 to 11 microns in diameter; chlamydospores, from 5 to 6 microns in diameter with terminal spores 5.5 by 10 microns; abundance of conidia, from 3.5 to 4 microns in width.

Endo's Medium (p_H 7.5): Growth similar to that on potato dextrose agar, demonstrating the aggregations of hyphae forming the spiny appearance; colony moist, the stain being absorbed by the mycelium and retarding growth; diameter of colony, 0.7 cm. after eleven days.

In addition to these mediums, the fungus was further grown on strongly acid and strongly alkaline broths to determine, somewhat, the physiologic preference of the organism. The acid culture was negative for growth, while the alkaline solution presented yeastlike cultures showing that, as would be expected, the parasite has an affinity for alkalinity.

Further physiologic and morphologic work is being carried on and will be published in the near future.

MORPHOLOGY

The organism was grown in hanging-drop cultures, the following fluid mediums being used: lactose broth, 2 per cent aqueous solution of preteose peptone plus glycerin, 2 per cent aqueous bacto-peptone and 2 per cent bacto-peptone plus 5 per cent meat extract. By observing the growth in these cultures, morphologic pictures could be easily obtained and drawn (fig. 4). To observe the structures more in detail, the fungus was transferred to a solution of glycerin and crystal violet stain (1 per cent aqueous), and allowed to stand for a while until, by observation, it was seen that the dye had penetrated the cell and the glycerin had cleared the material sufficiently. From twenty to thirty minutes was usually ample time for the operation. This method has proved successful on various occasions and as the internal make-up of the cell corresponded with that observed in a cytologic study of the original species (Endomyces capsulatus Rewbridge, Dodge and Ayers) being carried on at the present time, it was assumed that the picture observed was correct, so far as the species was concerned.

CLASSIFICATION

In our present state of mycologic taxonomy, fungi, such as the one being reported on in this paper, are in dire need of a definite classification. The medical literature is filled to overflowing with incorrectly applied generic names and fantastic specific designations, presenting thus a chaos which in the light of the ever increasing case discoveries is becoming a real problem. The latter fact is so, not because of the lack of knowledge on the part of the determiner, but simply to the inability of the laboratory workers to devote their time to the carrying out of determinations over a longer period. Organisms such as concern us at present take weeks and at times months for a stage in the life-cycle to be reached where sexuality can in any way be determined. Then again, yeastlike cultures have often been discarded, on developing a filamentous mycelium, because it was believed to be a contaminant and hence, we are left with a mass of names which cannot be associated with the original fungus.

The group of which Endomyces capsulatus, var. isabellina is a member, Endomycetales, is divided, on the basis of the characters presented, into three families: Dipodascaceae, the constituents of which, as pointed out by Gaumann and Dodge [34] have their basic principles involved in the life-cycle of the higher Phycomycetes; Endomycetaceae, in which we are particularly interested, having a variety of habitats and differentiations on the sexual life, shape and number of spores and morphologic characters, comprising the filamentous yeasts; and Saccharomycetaceae, or true yeasts, the group which is of great importance both economically and medically. In addition to these, there are many imperfect fungi, the life-cycles of which are not as yet known, and it is probable that when determined the members will be placed either in these or in some related genera or groups.

The genus, Endomyces, comes under the category of varied phenomena, since the species involved may be divided into two series based on the manner of copulation and reproduction. The first include forms in which isogamy plays the chief rôle with the sexual life degenerating to one of parthenogamy, while the second, the group which interests us, begins the series with heterogamy and degenerates also to parthenogamy, making the determination of an organism of the lower limits difficult.

For an intensive study of the group, the reader is referred to Gaumann and Dodge,[34] and for a discussion of this member of the Endomycetaceae, to Rewbridge, Dodge and Ayers.[12] The family, as

34. Gaumann, E. A., and Dodge, C. W.: Comparative Morphology of Fungi, New York, McGraw-Hill Book Company, Inc., 1928.

stated previously, has a varied life-cycle, habitat, manner of copulation, number and shape of ascospores and morphology, making a good classification of genera a problem yet to be worked out.

ANIMAL PATHOGENICITY

Two guinea-pigs, a mouse and a rabbit were used for study.

The mouse was given intraperitoneal injection with 1 cc. of the sediment of the spinal fluid obtained at the first lumbar puncture. For about two weeks it seemed sick, then gradually improved and seemed quite healthy. At the end of the six weeks it was killed. At autopsy there was no evidence of peritonitis, but the retroperitoneal lymph nodes were enlarged and soft. There were miliary abscesses in the lungs. Microscopic examination showed the encapsulated forms in lungs and lymph nodes.

A rabbit was inoculated intravenously with a broth culture. A four week old broth culture, measuring 80 cc., was centrifugated. The sediment was diluted to 2.5 cc. in physiologic solution of sodium chloride. One cubic centimeter was then injected into the left ear vein of the rabbit. A severe progressive infection developed, and the rabbit died in ten days. At autopsy both lungs were consolidated, showing myriads of miliary abscesses and punctate hemorrhages throughout. There was a small amount of clear pleural fluid. Examination of the pleural fluid in a hanging-drop preparation showed the organism. It also was found in exudate from the lung. The pleural fluid and lung were cultured, and an organism similar to that found at lumbar puncture obtained.

A guinea-pig inoculated intraperitoneally died six weeks later with a massive pneumonia. Microscopic studies showed the organism in the lungs and retroperitoneal lymph nodes. Another guinea-pig was shaved and the skin carefully cleansed. The skin was scarified, and sediment from the broth culture rubbed into it. At another site a few drops of the culture were injected into the skin. After six weeks there were no demonstrable skin lesions.

Summary.—1. A mouse inoculated intraperitoneally developed a generalized infection. Rewbridge Dodge and Ayers [12] caused a similar infection in mice by inoculation with their species of Endomyces capsulatus.

The encapsulated organism was demonstrated in the tissues of the mouse by microscopic examination.

2. A rabbit given intravenous injection developed a generalized infection with consolidation of both lungs, and died in ten days. The organism was found in the peritoneal fluid and exudate from the lungs at autopsy of the rabbit. Cultures from the lungs and pleural fluid of the rabbit showed the organism.

3. A guinea-pig inoculated intraperitoneally died after six weeks with a massive pneumonia. Budding yeastlike bodies were seen in sections of the lungs and retroperitoneal lymph nodes.

In Rewbridge, Dodge and Ayer's case, intravenous inoculation of a rabbit was without effect. Their organism was also apparently not pathogenic for guinea-pigs.

SUMMARY

1. The clinical record and autopsy observations in a case of meningitis due to Endomyces capsulatus, variety isabellina (new variety) are reported. It is worthy of note that the patient had had a so-called blastomycetic dermatitis for three years previous to the onset of the meningitis.

2. The organism was found in the spinal fluid, and cultured from the spinal fluid, urine and blood.

3. The morphologic and cultural characteristics of the organism are described.

4. The organism is pathogenic for mice, rabbits and guinea-pigs.

We are grateful to Mr. Morris Moore and Dr. Carroll W. Dodge of the Henry Shaw School of Botany for the privilege of appending Mr. Moore's report on the cultural characteristics of this new variety of endomycete.

Dr. Ralph Muckenfuss of the department of bacteriology, Washington University Medical School, and Miss Grace Mehrten of the bacteriology laboratory of Barnes Hospital, assisted in the study of the organisms and animal experiments. Mr. Walter G. Elle gave technical assistance in the preparation of the photomicrographs.

PSORIASIS AND MULTIPLE SUPERFICIAL EPITHELIOMA

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AND
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Arning,[1] of Hamburg, in 1922, bestowed the name "*multiplen Carcinoiden*" and Little,[2] of England, in 1923, the name "erythematoid benign epithelioma" on a condition which Wise, Fox, Fordyce, Whitehouse and others in the United States had for many years previously called "multiple, benign, superficial, flat epitheliomas."

The clinical features and differential diagnosis of this disease have recently been clarified and described by Fuhs,[3] Carol[4] and Wise,[5] and need not be repeated here, except to quote them as stating that the condition is a

> peculiar form of epithelioma, usually of the basal cell variety, but at times prickle cell and more rarely of the mixed, basal and prickle cell variety, of epithelial cell proliferation. It differs from other and better known forms of multiple epithelioma in that the lesions are essentially primary multiple formations which have their origin on normal skin; that is, they are not preceded by moles, warts, keratoses, arsenical keratodermas or by any other so-called precancerous manifestations of the skin.

This type of epithelioma is not infrequently confused with other forms of atypical, epithelial proliferation, such as Bowen's disease and extramammary Paget's disease and (more rarely) with arsenical epitheliomas and keratodermas. Wise stated that he had observed, over a period of six years, four cases of this disease which had been designated by others as Bowen's precancerous dermatosis. Fraser stated that he thought that probably more than half of the cases that have been

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1. Arning, E.: Ein Fall von multiplen Carcinoiden der Haut, Arch. f. Dermat. u. Syph. **138**:458, 1922.
2. Little, E. G. G.: Erythematoid Benign Epithelioma, Brit. J. Dermat. **35**: 435 (Dec.) 1923.
3. Fuhs, Herbert: Ueber die multiplen Carcinoiden der Haut, Acta dermat.-venereol. **7**:233, 1926.
4. Carol, W. L. L.: Ueber Carcinosis cutis multiformis (verrucosa), Arch. f. Dermat. u. Syph. **152**:686, 1926.
5. Wise, Fred: Multiple Superficial Benign Epithelioma of the Skin, Arch. Dermat. & Syph. **19**:1 (Jan.) 1929.

reported as Bowen's disease or so-called extramammary Paget's disease have undoubtedly been examples of multiple, superficial, benign epitheliomas.

Occasionally this disease has also to be differentiated from dermatoses other than those previously mentioned, such as lupus erythematosus, seborrheic dermatitis and psoriasis, which sometimes bear a superficial resemblance to it. As far back as 1910, Fordyce,[6] and, more recently, Sequeira and Wise, have called attention to this occasional resemblance. Incidentally, Little also stated that lupus erythematosus was the diagnosis universally offered in the first of the seven cases he had reported.

It is the purpose in this paper to report five cases of superficial epithelioma occurring in patients with psoriasis but not involving the psoriatic patches. Two of the patients were seen in the dermatologic clinic of the Temple University Medical School and Hospital and three in the private practice of one of us (Dr. Wright). Up to the time that these patients were seen by us, all of them had had psoriasis for many years, and in all of them the cutaneous epitheliomas that had developed on previously sound skin bore a superficial resemblance to the patches of psoriasis.

The occurrence of an epithelioma in a patch of psoriasis is not unknown. Fordyce [6] observed that chronic diseases of the skin, such as lupus vulgaris, lupus erythematosus, Darier's disease, seborrheic dermatitis and psoriasis, offer favorable bases for the development of epithelioma, and he reported a case in which multiple tumors of the basal cell type were present. (He did not specify, however, whether or not they occurred in the patches of psoriasis. Presumably they did.) Metastases subsequently developed, and the patient died of carcinoma.

Hardy declared that he had seen cancer develop so frequently in persons affected with psoriasis that he believed in a certain connection between the two maladies, a belief in which Bazin concurred. Flint and Gordon,[7] Whitfield [8] and Gray [9] reported instances in which epithelioma developed on patches of psoriasis. Sequeira [10] stated that he had had

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6. Fordyce, J. A.: The Pathology of Malignant Epithelial Growths of the Skin, J. A. M. A. **55**:1624 (Nov. 5) 1910.

7. Flint, E. R., and Gordon, J.: A Case of Squamous Carcinoma of the Scalp, Associated with Two Rodent Ulcers on the Shoulder Originating in a Patch of Psoriasis, Brit. J. Surg. **16**:321 (Oct.) 1928.

8. Whitfield, A.: Brit. J. Dermat. **18**:40, 1906.

9. Gray, A. M. H.: Rodent Ulcer Occurring in a Patch of Psoriasis in the Gluteal Cleft, Brit. J. Dermat. **24**:325, 1912.

10. Sequeira, J. H.: Diseases of the Skin, ed. 4, London, J. & A. Churchill, 1927, p. 558.

several cases of multiple benign epithelioma occurring in persons with a history of psoriasis or seborrheic dermatitis, but he did not mention whether the lesions developed on diseased, healed or sound skin.

Many patients with psoriasis are treated with arsenic at some time in the course of the disease, usually in the form of solution of potassium arsenite. When long continued, this treatment may result in the development of arsenical keratoses, which is followed in some cases by (secondary) epitheliomatous changes. Hartzell [11] reported eleven cases of epithelioma as a sequel of psoriasis, one of which was his own. In all but three, some form of keratosis was a marked accompanying feature, and the epitheliomas occurred either in the patches of psoriasis or in the patches of keratosis. He believed that the arsenic used in the treatment of the psoriasis was largely responsible for the development of both the keratosis and the epitheliomas.

Two, and possibly three, of the patients in Little's original series of seven cases had psoriasis. He therefore noted that "there has been a curious frequency of a history of psoriasis in several cases reported," and he further observed that "the association is probably accidental, and there is no evidence of a patch of erythematoid epithelioma arising in the site of a patch of psoriasis."

Our cases support this observation of Little and the more recent one of Wise to the effect that the lesions of this disease "have their origin on normal skin."

Hartzell reported ten cases besides one of his own which he believed comprised all of the cases up to 1899. They present a remarkable uniformity in the clinical features and course. In all the psoriasis was of long duration, usually many years. In all but three some form of keratosis was a marked feature, appearing after a variable period and most frequently on the palm and sole in cornlike excrescences; finally cancerous ulceration began beneath one or more of them. In eight of the eleven cases in which mention is made of the treatment of the psoriasis arsenic had been given in considerable quantity for a long period, and in view of its almost universal use in this malady, its administration in the remaining three cases cannot be positively excluded. In 50 per cent of the cases the ulcerative lesion was multiple and in half of the cases also the cancerous ulceration appeared before the patient was 40 years of age, occurring in one patient at the age of 25. It was Hartzell's contention that the early appearance and the multiple character of the carcinoma accompanying psoriasis would seem to point to some special etiologic factor, which he believed was the arsenic used in the treatment of the psoriasis.

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11. Hartzell, M. B.: Epithelioma as a Sequel of Psoriasis and the Probability of Its Arsenical Origin, Am. J. M. Sc. **118**:265 (Sept.) 1899.

A brief review of the literature reviewed by Hartzell [11] is herewith presented.

He reported a case of psoriasis in a woman aged 35; the condition had been present since the age of 14. Horny patches and cornlike elevations developed on the palms and soles (the patient took arsenic in considerable doses over long periods). Finally ulcers developed on the left heel. These were followed by metastatic growths in the groin and death.

Hartzell stated that Pozzi recorded the first case of epithelioma associated with psoriasis in 1874. In 1877, Cartaz reported the second case of epithelioma occurring in a patch of psoriasis. In 1885, J. C. White reported two cases of long standing psoriasis followed by wartlike growths in psoriatic patches, which terminated in carcinoma. Jonathan Hutchinson, in 1887, reported three cases of psoriasis which terminated in carcinoma. The patients had taken liberal quantities of arsenic. Hans Hebra reported a case of multiple epitheliomatous lesions occurring in a man who had had psoriasis for many years; psoriatic patches had appeared which had assumed a warty character. No details as to the treatment of the psoriasis were given by Hebra. Geyer referred to a case reported by Power of carcinoma of the hands arising from a placque of psoriasis.

REPORT OF CASES

CASE 1.—*History.*—Mrs. M. H., a white woman, aged 60, had had psoriasis since the age of 45. At the age of 48, she first noticed a small reddish patch about half the size of a silver dime over the lumbosacral region, but at the time she regarded it as a part of the psoriatic eruption. This patch gradually but persistently increased in size. No symptoms were associated therewith until 1929, when a burning pain developed, which persisted. When the patient was 55, a second lesion developed on the left side of the abdomen about 3 inches (7 cm.) above the iliac crest in which subsequently a persistent burning, painful sensation developed.

Examination.—Examination revealed that the larger of the two lesions, located over the lumbosacral part of the spine, was an irregular, sharply marginated, dull red patch about 8 cm. in diameter. The surface was dry and covered here and there with a thin layer of slightly adherent, grayish-yellow scales and some blood crusts. The entire patch was superficial; there was no infiltration or thickening of the underlying tissues. It had a sharply defined, raised border, which was pearly pink and about from 0.5 to 1 mm. in thickness.

The patch on the abdomen presented the same general characteristics; it was somewhat oval, measuring about 5 cm. in length and 4 cm. in width.

The patient gave no history of having taken arsenic for the treatment of the psoriasis.

Microscopic Data.—Microscopic study of a section (fig. 1) from the lesion on the back revealed a thin covering of stratified squamous epithelium. The epithelial pegs were numerous and moderately thickened. In the right area of the section, there was an exaggerated peg forming a large flask-shaped mass. This mass consisted of polyhedral cells with round nuclei; it was poor in chromatin and possessed

a large, pale-staining nucleolus. Numerous mitotic figures were seen. The peripheral cells of the mass were continuous with the basal cells of the normal covering, and, like them, were for the most part columnar. This condition was a pure basal cell carcinoma.

CASE 2.—*History.*—H. F., a white man, aged 45, had had psoriasis continuously since the age of 7 years. About 1924, he first noticed a reddish elevation on his back over the left scapula; this lesion was painful on pressure. It spread slowly peripherally, was asymptomatic, and, unlike the patches of psoriasis, did not disap-

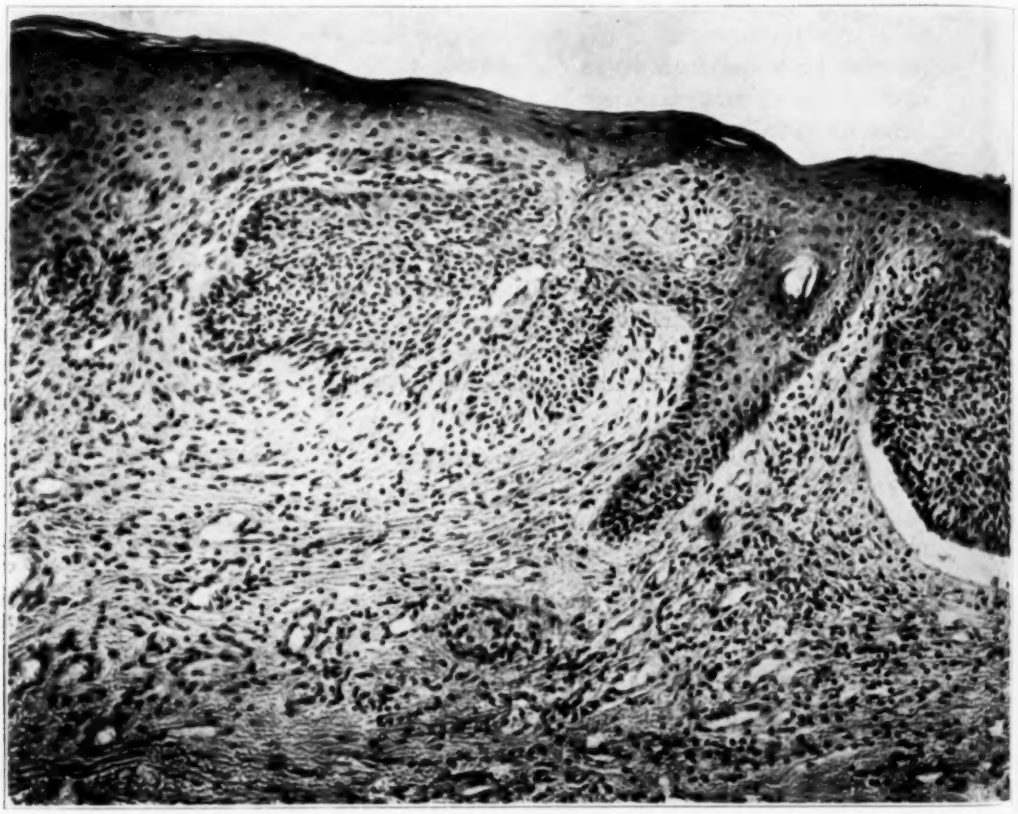

Fig. 1.—Photomicrograph showing multiple superficial, basal cell epithelioma.

pear but remained fixed. Similar permanent lesions appeared at irregular intervals, until at the time of the first examination he had twelve lesions of various sizes and shapes, seven on his back (fig. 2), three on his left arm, one on his chest and one on his left temple.

These lesions presented the same physical characteristics as those in case 1, except that the center of the lesion first to develop (the one over the left scapula) ulcerated in 1930 and developed into a raised, sharply marginated, fungating growth. It was for this ulcer that the patient was referred by his family physician to the clinic for treatment, the underlying lesion having been considered with the other similar lesions as a manifestation of psoriasis.

The patient stated that he had taken "drops" for the treatment of the psoriasis about fifteen years previously for about six weeks, and that he had not taken them since. Study of biopsy material for the presence of arsenic gave negative results.

Microscopic Changes.—Three biopsies were made in this case from three different lesions. The tissues were prepared and sections made in the laboratories of Dr. Konzelman of Temple University Medical School.

The histologic picture was the same in all of the sections. The epidermis was generally thin. Each of its layers was represented. There was no hyperkeratosis. One section showed ulceration. The surface in this section was represented by tumor cells and leukocytes. Near the site of the tumor the epithelial pegs were

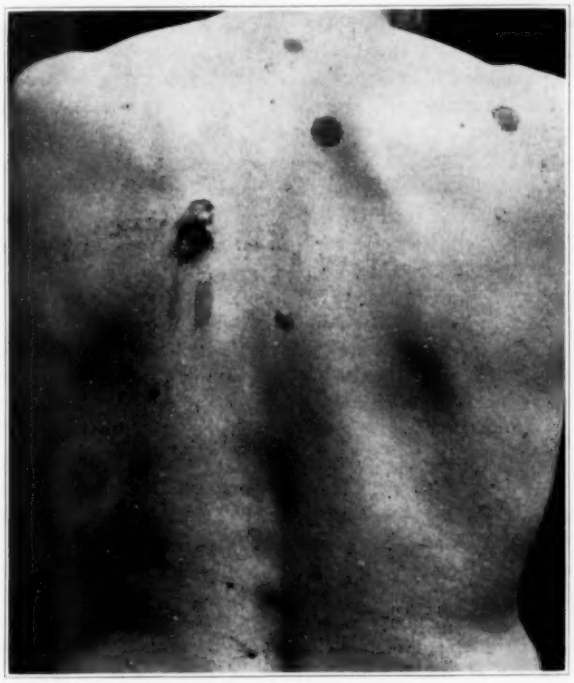

Fig. 2.—Multiple superficial epithelioma of the back in case 2. Note the resemblance to psoriasis.

longer and broader, but their architecture and the arrangement of the cells were otherwise normal. The pegs were increasingly longer and larger until several large masses of cells extended deep into the corium. In each of these masses the peripheral cells were arranged in an orderly manner as columnar elements, corresponding to the orderly basal cells of the malpighian layer. The centrally placed cells in the masses were so densely packed that their outlines could not be determined. Mitotic figures were rare. This growth was determined to be mixed basal cell and squamous cell epithelioma.

In another section the surface stratified epithelium was stretched over a large mass lying within the corium. This mass was composed of several small groups of deep-staining cells; they were within spaces in the stroma, the lining of which

consisted of denser collagen fibers than that of the more distant stroma. The cell masses in this section originated in the epithelial pegs of the surface layer. Mitoses were infrequent.

A third piece of tissue was prepared according to the technic suggested by Osborne for the demonstration of arsenic, but its presence could not be detected.

Case 3.—Mr. F. J., aged 37, was first seen by Dr. Jay F. Schamberg in 1929, at which time the patient presented numerous patches of psoriasis over the trunk and a few in the scalp. There was no history of his taking arsenic in any form. In fact, he had had no previous treatment except ointments, although he had had the eruption for fifteen years. He was seen by one of us (Dr. Wright) in May, 1924, at which time he presented three lesions over the trunk, which, although superficially resembling the patches of psoriasis, on close examination were seen to be superficial epitheliomas. These lesions were treated with carbon dioxide snow and were completely cured. Biopsy was not performed in this case. This patient has been seen at intervals of from one to two years, and several subsequent epitheliomas have been similarly treated. Examination revealed no arsenical keratoses or pigmentation.

Case 4.—Miss E. F., aged 40, was first seen in 1925, at which time she presented scattered patches of psoriasis over the scalp and back. She also presented on the forehead an oval, elevated lesion, 1 inch (2.5 cm.) by 2 inches (5 cm.) in diameter, and a similar lesion over the lower part of the back 3 inches (7 cm.) by 5 inches (12 cm.) in diameter, which were diagnosed as superficial epitheliomas. These lesions were dull red, in this respect resembling closely the patches of psoriasis, but the borders were definitely elevated, rolled out and, in places, pearly. The patient gave a history of taking arsenic over a considerable period in previous years. The superficial epitheliomas were destroyed by electrodesiccation. In July, 1931, she was again seen, and a new lesion on the back was destroyed by electrodesiccation. She presented no arsenical pigmentation or keratoses.

Case 5.—Mrs. W. H. McG., aged 60, was first seen in July, 1931, at which time she presented scattered patches of psoriasis over the scalp, back and legs. On the right side of the chest, the left side of the neck and the left leg she presented three lesions, which were recognized as superficial epitheliomas. There was a slight erosion of the lesion on the leg and a history of bleeding on traumatization. The epitheliomas on the neck and chest were treated with heavy doses of roentgen rays, and they disappeared within three months. The larger lesion on the leg was destroyed by electrodesiccation and healed completely, leaving a smooth purplish-red scar. The patient stated that she had had psoriasis for thirty-three years, and that the lesion on the leg, which she recognized as being "different" in type, had appeared thirteen years before she was seen by us. She had been given arsenic over a long period during 1910 and 1911. There were no arsenical keratoses nor any arsenical pigmentation of the skin.

COMMENT

In reporting these five cases of multiple superficial epitheliomas associated with psoriasis, we are not claiming that there is a direct relationship between the two conditions, but wish to call attention to the possibility that the epitheliomatous lesions may be overlooked or regarded as part of the psoriatic eruption. Wise has called attention to the occasional association of these two diseases, and Pfahler, in a presentation at the Philadelphia Dermatological Society in 1929, presented

several cases of multiple superficial epithelioma which had been incorrectly diagnosed and treated as psoriasis by other physicians.

It was our first opinion that the previous taking of arsenic for the treatment of psoriasis might be the cause of the epitheliomatous lesions, but no arsenic could be demonstrated in the sections prepared according to the technic of Osborne. On the contrary, arsenic is easily demonstrable in the keratoses frequently seen in patients with psoriasis who have taken considerable amounts of arsenic in previous years. Not one of our patients had arsenical keratoses or pigmentation.

KERATODERMA DISSEMINATUM PALMARIS ET PLANTARIS

ITS MODE OF INHERITANCE

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In this article, only the idiopathic variety of disseminate palmar and plantar keratoderma is considered. This variety may be familial or nonfamilial; the familial cases are represented by those originally described by Brauer [1] under the title keratoma dissipatum hereditarium palmare et plantare, and the latter, by those first recorded by Buschke and Fischer,[2] with the designation keratodermia maculosa disseminata palmaris et plantaris. Whether or not these titles should be accepted as synonyms for a single clinical entity has been a matter of some controversy, but most authors (Fuhs, Rinsema, Sklarz and Neuber) favor the affirmative view.

The clinical and histologic characteristics of the anomaly are well known through the papers of Sweitzer [3] and Lieberthal [4] in this country and by those of Fuhs,[5] Brann,[6] Sklarz,[7] Rinsema,[8] Galloway,[9] Balzer [10] and Neuber [11] in foreign countries. This list comprises only some of the more important communications appearing in fairly recent years.

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1. Brauer: Arch. f. Dermat. u. Syph. **114**:211, 1913.

2. Buschke and Fischer: Ikonographia Dermat. **5**:183, 1910.

3. Sweitzer, S.: Keratoma Punctatum, Arch. Dermat. & Syph. **8**:687 (Nov.) 1923.

4. Lieberthal, D.: Disseminated Palmar and Plantar Keratoderma, Arch. Dermat. & Syph. **14**:655 (Dec.) 1926.

5. Fuhs, H.: Zur Kenntnis der herdweisen Keratosen an Händen und Füssen, Acta dermat.-venereol. **5**:11, 1924.

6. Brann, G.: Ein Beitrag zum Keratoma palmare et plantare hereditarium (Keratoma dissipatum Brauer), Arch. f. Dermat. u. Syph. **139**:201, 1922.

7. Sklarz, E.: Keratodermia maculosa disseminata symmetrica palmaris et plantaris, Arch. f. Dermat. u. Syph. **144**:295, 1923.

8. Rinsema, P. G.: Sur la kératodermie maculeuse disséminée symétrique, palmare et plantare (Buschke-Fischer), Acta dermat.-venereol. **6**:299, 1925.

9. Galloway, J.: Punctate Keratoses of Palms of Hands and Soles of Feet, Brit. J. Dermat. **30**:123 (July-Sept.) 1918.

10. Balzer, F.: Contribution à l'étude de la dermatose dite kératome ou keratoderma ponctiforme ou miliare, Ann. de dermat. et syph. **6**:225, 1925.

11. Neuber, E.: Disseminierte Keratodermien an den Handflächen und Fussohlen, Arch. f. Dermat. u. Syph. **162**:197, 1930.

Up to 1926, Lieberthal was able to collect twenty-seven cases from the literature and added one of his own. To these may be added five cases published at about the same time by Fuhs.[5] Since that time a number of cases have been presented at society meetings, but few formal papers with casuistic material have appeared.

It appears to me that further clinical reports, unless they present something atypical, are no longer required. What is needed is more light on the mysteries of etiology and pathogenesis which surround this dermatosis.

For these reasons, when the opportunity arose to see a typical case, I began an inquiry into the inheritance of the anomaly and have been able to trace it through six generations of my patient's family. This report is based on the information thus obtained. The following personally observed case formed the starting point of the inquiry.

REPORT OF CASE

History.—G. T., a man, aged 35, was first seen by me on Sept. 25, 1931, with the complaint of "warts" on his palms and soles. The lesions had appeared first when he was about 18 years old. As they occasioned no special discomfort and did not interfere with his occupation (postoffice employee), he had never previously sought medical advice. The onset was insidious, and his recollection of it may have been somewhat faulty, but he believed that the lesions appeared first on both palms and later on the soles.

In the early years of the disorder, the lesions were few, but slowly and steadily new ones appeared, and as the older ones never seemed to disappear, they gradually amounted to a considerable number. The patient described the individual lesion as beginning as a tiny hard point which gradually developed into the large hard callus-like papules which studded his hands. He stated that he had often picked out the small horny "seeds" and noted that some of them showed a threadlike appendage about one-eighth inch (0.3 cm.) long which came away with them. Once in a while, after hard labor, the lesions became somewhat tender and painful, though never enough to interfere with his activities.

His father had died of pneumonia at the age of 65. His mother was 65 years old and was in good health. One brother had died in infancy. Three brothers and two sisters, all adults, were in good health.

To the patient's knowledge there had been no tuberculosis, syphilis or endocrine diseases in the family. He knew that other members of his family had the dermatosis of which he complained. The record of this will be given.

Besides influenza in 1918, the patient had never been ill. He said that he had not had venereal diseases. Besides his present occupation, he had been an aviator, and gave lessons in flying in his spare time. He had dermatophytosis of the feet up to 1929. This had disappeared after the use of a proprietary keratolytic. He had never taken arsenic and, in fact, never more than a few doses of medicine.

Examination.—Physical examination showed the patient to be slender, but well nourished and muscular. He was 5 feet and 8 inches (172.7 cm.) in height and weighed 122 pounds (55.3 Kg.). A general physical examination revealed no noticeable abnormalities. With the exception of the palmar and plantar lesions, his skin showed nothing abnormal. Cutaneous sensation in all areas was normal.

Urinalysis and blood counts gave normal results. The Wassermann and Meinicke reactions were negative. A basal metabolic test gave a value within normal limits.

The lesions were present on the palms and soles as well as on the lateral surfaces of the heels. There was quite a marked symmetry in their distribution and in the relative size of the lesions in corresponding locations. The lesions showed no relation to any glandular structures and, except for the papules, the skin of the palms and soles was soft and flexible. There was no hyperhidrosis. The nails were normal in appearance.

The smallest and presumably the earliest lesions were simply firm, minute punctae (fig. 1). As the lesions reached a somewhat larger size, they consisted

Fig. 1.—Palmar lesions in my patient. Note their distribution on the areas subject to pressure. The tips of the fingers showed especially numerous papules, probably accounted for by the fact that the patient had written a great deal on a typewriter.

of a small, hard, yellowish, seedlike body, which on removal left a shallow cup-shaped depression. Their sites of predilection were the pulps of the fingers, though a few were scattered on the palmar surfaces of the fingers and on the palms.

The largest lesions, which were fewer in number than the foregoing ones, were quite prominent, wartlike, yellowish papules. The central core, of almost stony hardness, was firmly fixed, and could be removed only by paring it down with a sharp knife. The thick outer wall, which embraced this core, sloped precipitously to the level of the normal skin. These lesions were present especially on the hypothenar eminences, at the proximal area of the palms adjacent to the wrists and at the roots of the fingers, though a scattered few appeared on the flexor

surfaces of the fingers. These lesions, as well as the smaller ones, appeared to develop particularly on areas subject to pressure. For example, the center of the palms (one small lesion excepted) and the soles beneath the instep were not invaded. There were somewhat over a hundred lesions on each hand and foot.

Relatively, there was a greater number of the larger lesions on the soles than on the palms. There was no essential difference between the efflorescences on the palms and the soles. The large lesions on the soles were flattened and somewhat softer than those on the palms, probably as the result of pressure and moisture. The largest lesions were on the lateral surfaces of the heels.

Course.—The patient had been under observation for about eight months. During this time he received several subintensive roentgen treatments, keratolytics and magnesia by mouth and locally. These measures, which were used without any hope of success, produced no appreciable change in the condition.

Histology.—Two pieces of tissue were removed from the palm. One piece contained two lesions; one was the smallest lesion noted (half the size of a pinhead), and the other was somewhat larger. The other specimen contained the largest lesion on the palms. After embedding in paraffin, they were stained with hematoxylin-eosin. The piece with the two small lesions was cut serially.

In the section containing the small lesions, the cutis showed no abnormalities. The smallest lesion appeared as a shallow indentation of the rete, covering the space of about four papillae. The papillae were obliterated in the center, but the rete was approximately normal in width. The individual cells of this layer showed no pathologic alterations. Toward the center the granular layer was increased (from 4 to 6 cells in width). There was a moderate hyperkeratosis, the horny layer being widened by sinking into the depression as well as slightly protruding above the surface.

The most interesting feature of this lesion was its intimate association with the mouth of a sweat duct (fig. 2). This sweat duct, which disclosed nothing abnormal, opened at the center of the lesion. The sweat glands were normal.

The other lesion in this section was simply a larger edition of the former one. It occupied the space of about ten papillae. It was situated at the edge of the section, and the punch which removed the piece had sliced away part of the cutis beneath it, but under a portion of it there still remained tissue down to the level of the sweat glands. A sudoriparous gland and its duct in this area were apparently normal. The only deviations from the normal were a moderate hypergranulosis and a pronounced hyperkeratosis. Here, too, the widened corneous layer was sunk into a depression, while its surface was, in part, eroded. There were four sweat ducts in close association with this lesion, two immediately adjacent and two opening in the lesion.

The largest lesion was cut too shallow and showed nothing below the papillary body. Many of the papillae and their corresponding pegs were long and narrow. On the periphery of the lesion these long pegs recalled the crab-claw appearance described by Brauer.

The papillae contained a moderate infiltration of lymphocytes. There was a pronounced acanthosis with some areas in which many of the cells showed perinuclear hydrops and most of the others were swollen. The granular layer was widened at the periphery of the lesion, but in the central depression it was absent, and in this area there was parakeratosis, while on the outer slopes only hyperkeratosis was seen. There was an enormous hypertrophy of the corneous layer.

The histologic features that have been noted deserve some comment. Particularly is this true of the smallest lesion because of its situation at

the outlet of a sweat duct. Study of the serial sections showed that this duct opened at the center, or approximately the center, of the lesion. So far as can be determined from the literature available to me, only Brann has previously noted the periporal site of a lesion.

Parakeratosis has been noted by others (Brauer, Fuhs and Matsumoto [12]), though the usual finding is pure hyperkeratosis. Brauer thought that the presence of parakeratosis in his case was of some value in differentiating it from the Buschke-Fischer type, but it seems to me

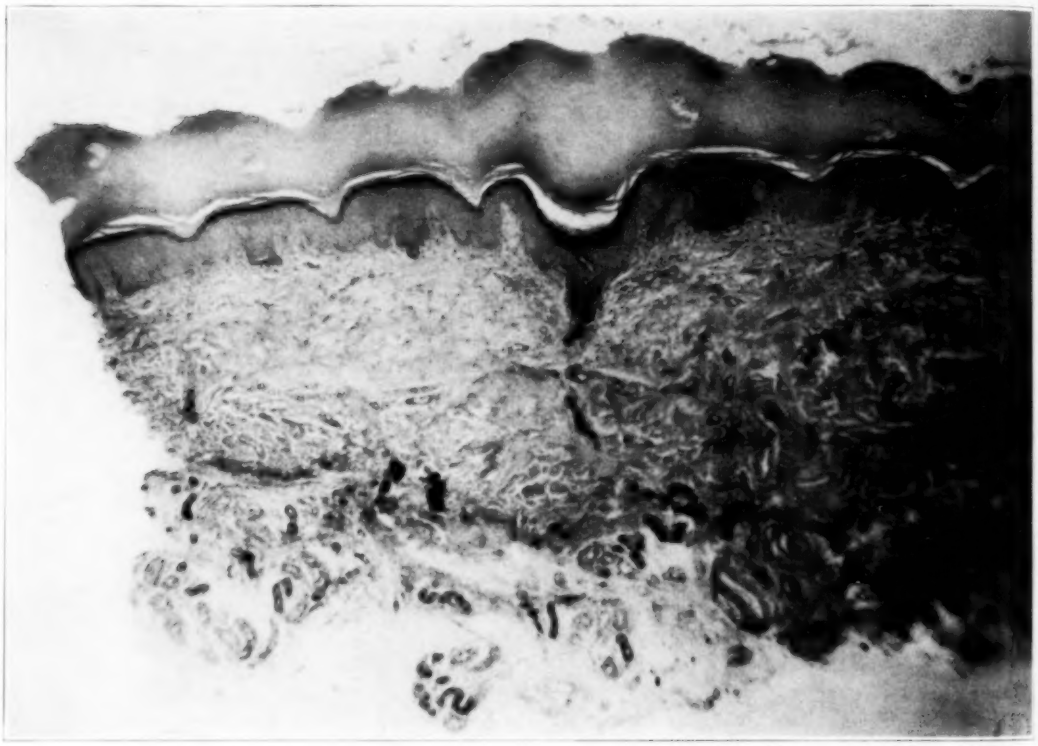

Fig. 2.—Center of the smallest lesion, revealing its relation to a sweat duct. There is moderate hypergranulosis about the orifice.

that parakeratosis is not an inherent feature of the lesion but simply the consequence of a mild inflammation produced by trauma, in the same way as the base of a corn becomes inflamed in a tight shoe. The situation of the parakeratosis in the largest lesion (over the deepest part of the depression) seems to me to favor this assumption.

12. Matsumoto, S.: On a New Form of Punctiform Keratoderma, J. Cutan. Dis. **36**:280, 1918.

Summary of Case.—The foregoing case is a classic example of a well developed instance of the disseminate type of palmar and plantar keratoderma. The anomaly first appeared at 18 years of age, and since then there had been a steady accretion and progress in the size of the lesions. Though developing as a delayed case, there was nothing in the patient's history or examination to occasion a suspicion of an acquired disease. The diagnosis in this case was so obvious that a differentiation from other diseases appeared unnecessary.

The anomaly has been traced through six generations of the patient's family (fig. 3). To save space, details concerning the family pedigree

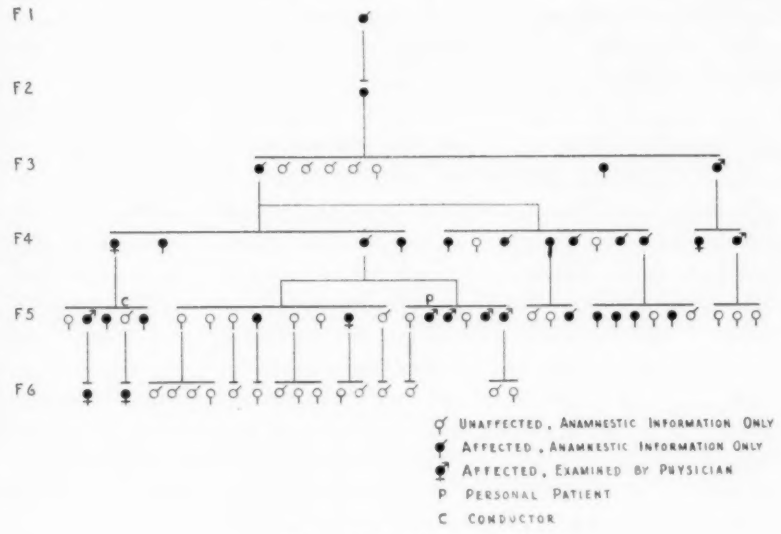

Fig. 3.—Genetic chart.

are omitted. However, mention must be made of the last generation, in which seventeen persons have been located. Fifteen of the seventeen are between the ages of 20 and 40, while two are quite young children. One of the affected children in this (*F 6*) generation has a nonaffected father, the only instance of a conductor in this family. It is questionable, however, because this person was not examined by a physician. Conductors in dominant inheritance are well known; Koehler [13] stated that conductorism in dominant inheritance varies within wide limits; in some families none appear; in others, up to 33 per cent.

The information at my disposal concerning this family is for the most part anamnestic. The family is scattered over a great part of the United States, and it has therefore been impracticable to see personally

13. Koehler, O.: Vererbungsforschung in der Dermatologie, Arch. f. Dermat. u. Syph. **160**:10, 1930.

any but the patient whose case I have recorded. However, twelve of the affected members have been examined by physicians at my request. Brief reports of the clinical condition have in this way been made available. Of those who were not seen by physicians, it seems reasonable to believe that the information regarding them is correct. In the first place, this anomaly is one which obtrudes itself, and in the second, in each instance in which I have been able to check a person's statement by a physician's examination, the latter has corroborated the former.

This family is of pioneer American stock, of a social plane which may be called middle class. It is composed for the most part of farmers and small town dwellers. The sprinkling of urban dwellers follow the occupations of tradesmen or clerical workers, with two in professional careers. There has been no intermarriage in this family, nor have any of the affected members married a person with the anomaly.

HEREDITY IN THE CLINICAL FORMS OF KERATODERMA PALMARIS ET PLANTARIS

Of the clinical varieties of this anomaly, the diffuse form has been extensively studied as to its mode of inheritance. Siemens,[14] whose investigations of inheritance in cutaneous diseases occupy first rank, called it a paradigm of dominant inheritance among the dermatoses. Brunauer,[15] who collected all pedigrees that had been published up to 1923, corroborated Siemens' statement. However, it must be stated that a few cases are on record which show a recessive mendelism (Leven [16]). This indicates, as has been shown by Siemens [17] for other dermatoses, that one phenotype may represent two or more genotypes.

Siemens [14] has recently reported several family trees of the striate type in which the mode of inheritance was dominant.

Investigations of the mode of inheritance in the disseminate type are meager. Brauer's original cases comprised a group of nine persons, three brothers and their six sons. Sex linkage seems indicated, but the information is too scarce to permit any definite deductions. Brann's [6] family tree comprised three generations—grandfather, son and the latter's three daughters—and the type of inheritance cannot be definitely

14. Siemens, H. W.: Keratosis palmo-plantaris striata, Arch. f. Dermat. u. Syph. **157**:392, 1929; also in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1927, vol. 3, p. 109.

15. Brunauer, S. R.: Zur Vererbung des Keratoma hereditarium palmare et plantare, Acta dermat.-venereol. **4**:489, 1923.

16. Leven, L.: Erblichkeitslehre mit besonderer Berücksichtigung der Dermatologie, Zentralbl. f. Haut-u. Geschlechtskr. **25**:1, 1928.

17. Siemens, H. W.: Virchows Arch. f. path. Anat. **238**:200, 1922; abstr., Zentralbl. f. Haut- u. Geschlechtskr. **6**:246, 1923; Vererbungsforschung in der Dermatologie, Arch. f. Dermat. u. Syph. **160**:37, 1930.

deduced. Fuhs [18] recently recorded nine cases in nine families, the record in each family showing only two generations (the parents and their children). As the disease had appeared in each generation and the total number of affected to unaffected showed a relation approximating 1 : 1, Fuhs concluded that there were well founded indications of inheritance as a regular dominant.

The family tree which is reported herein, therefore, is the most extensive so far reported, and is the first single family in which the type of inheritance could be definitely determined. It will be noted that no generation has escaped.

Again, only affected parents have transmitted the anomaly, with the exception of the conductor already mentioned.

For estimating the numerical relation, the two affected persons in the *F 1* and *F 2* generations and the two young children in the *F 6* generation should be excluded. This leaves all known siblings over the age of 15 (the earliest age of expectancy in this family) for the calculation. Among these people there are thirty-one affected and thirty-seven unaffected, which is quite close to the theoretic ratio of dominant inheritance of 1 : 1.

The three cardinal points of dominant inheritance are: no generation should escape; only affected persons transmit the trait (a certain proportion of conductors are permissible), and the ratio of affected to unaffected persons should approximate 1 : 1. As these points are exemplified in this family pedigree, it is concluded that the anomaly is inherited as a regular dominant.

There were eighteen affected female and fifteen affected male members of the family. Neither sex linkage nor sex limitation appears.

In every case in this family, the anomaly presented only the pure papular form. The clinical manifestations varied to a considerable extent, so far as their degree of development was concerned. According to the anamneses as well as the examinations by physicians, the cases varied from what might be termed larval forms (two lesions on a palm) to full blown examples, such as that presented by my case. The presence of larval or abortive cases in this family tree is of interest, since one of the valuable contributions of genetic studies in cutaneous diseases has been the recognition of larval forms of various dermatoses. Certainly, from what has been written me of the case mentioned in which there were two lesions, I doubt that its true nature would have been recognized if it had not been known that the anomaly was present in the patient's family.

For an inherited condition, the age at onset of the disseminate type of palmar and plantar lesions is inexplicably delayed. Usually the

18. Fuhs, H.: Der Erbgang der Keratosis palmo-plantaris papulosa (H. W. Siemens), Arch. f. Dermat. u. Syph. **160**:52, 1930.

disease appears in late childhood or in the postpubescent period. In the family which I have recorded, definite information on this point was obtained from ten affected persons, and the age of onset in all was at least 15. The following tabulation shows the results of this inquiry:

Age at Onset	No. of Patients
15	1
18	1
20-30	3
30-40	4
45	1

Undoubted inherited cases appearing as late as these have been reported by Fuhs, Brauer and Brann (from 20 to 30 years), Callomon (42 years; quoted by Fuhs [5]), Lieberthal (43 years) and Neuber (from 45 to 47 years). Neuber's case is questionable, since the family history was unobtainable. In nonfamilial cases the disease has appeared even later than this, Fuhs stating that Riehl's patient was 60 years old when it developed.

The tardy onset of an inherited condition naturally brings up the question whether extraneous factors have a part in the process. In this regard, the chief factors that have been invoked are endocrine and neurotrophic disturbances and infectious diseases, chiefly syphilis. In my patient, as well as in several other members of his family, no basis for invoking any of these factors as a contributing cause was found. Examinations of these persons, however, was not sufficiently complete to permit absolute denial of such a possibility. In my patient I should regard the influence of external factors, especially pressure, as having an influence in determining the site and fullest development of the lesions, since the most prominent lesions were present on areas such as the heels and balls of the feet, the hypothenar eminence and other eminences of the hands especially exposed to traumatism and pressure. Environmental factors, such as climate, locality or occupation, could be excluded with a reasonable degree of certainty.

Postowsky [19] has recently reported familial cases of the diffuse type associated with endocrine-autonomic disturbances which he regarded as definitely contributory. However, it seems to me that not much is known in regard to this question, and that, barring the physiologic activity of the endocrine and nervous systems, only in isolated cases can a neurotrophic or endocrine factor be considered. None of these cases has been of the papular (disseminate) type, but this is of no particular moment, since, in my opinion, the pathogenesis of the various types of keratoderma is quite similar. In stating this, however, I do not wish to be understood as regarding the genetic disturbance (mutation) that

19. Postowsky, D.: Zur Frage der Ätiologie der hereditären symmetrischen Keratodermie, Acta dermat.-venereol. **11**:305, 1930.

originates the anomaly as being identical in each of its clinical forms. From what is known of gene disturbances in the fruit fly (Drosophila melegaster), it may be inferred that in man a diffuse keratoderma is the result of a different mutation than that causing papular keratoderma. Apparently, manifestation disturbances with or even without polyidism may play a rôle in producing in the one case a diffuse, and in the other a papular, type, or even a combination of forms, such as has been noted by Siemens [20] in the striate variety (pure striate and diffuse and striate forms with changes in the nails in the same family), designated by that author as heterophenism.

Siemens felt that he had demonstrated polyidism in these cases. He did not think that environmental (paratypic) influences played a part. Vohwinkel,[21] on the other hand, believed that predisposition was an important factor in the production of the various clinical manifestations of the anomaly. According to this thesis, the predisposition to the formation of keratoderma is inherited in different intensity, so to speak. For instance, the papular form indicates a lesser degree of predisposition than the diffuse form. This hypothesis, according to Vohwinkel, dovetails with the clinical observation that diffuse forms appear earlier in life than papular forms. It likewise offers an explanation as to why, in the family on which I am reporting, with the pure papular type, the age of onset was so delayed.

This hypothesis, which accords a great rôle to idiodisposition, is intriguing but must, for the present, remain *sub judice.*

Clinical combinations, however, did not occur in the family reported by me, for, as previously mentioned, all cases showed the pure disseminate type. For this reason, as well as the fact that environmental and systemic factors were apparently absent, the anomaly may be regarded as inherited as the consequence of a single gene disturbance; in brief, as simple.

COMMENT

The question as to the relation between the familial and the nonfamilial cases has always been puzzling. Authors who consider these varieties as identical point to anamnestic difficulties as perhaps explaining the nonfamilial cases, especially as in many patients the anomaly appears relatively late in life. It is my feeling that perhaps two other reasons may be invoked in explanation of the nonfamilial cases. The first is that the anomaly (phenotype) may be transmitted by different modes of inheritance, some of them being so irregular that they defy investigation in the human race. This is already indicated by the reports collected by Leven. The second thought is that some of the nonfamilial

20. Siemens (footnotes 14 and 17).

21. Vohwinkel, K. H.: Keratoma hereditarium mutilans, Arch. f. Dermat. u. Syph. **158**:354, 1929.

cases represent the original mutant. There is every reason to believe that the mutation which gives rise to the anomaly is still appearing in the race, and hence isolated cases which represent this fact are coming, quite rarely of course, to observation.

CONCLUSIONS

1. The clinical and histologic features of keratoderma disseminatum palmaris et plantaris are well known, while its etiology and pathogenesis are quite obscure.

2. In this article some light is thrown on the latter questions by a study of its mode of inheritance.

3. A typical case and the patient's family pedigree through six generations, comprising sixty-eight persons above the age of 15 years, are reported.

4. In all cases in this family the disease was of the pure disseminate type.

5. Previous reports in the literature on the mode of inheritance of the disorder are meager, but indicate its inheritance as a dominant.

6. The present study reveals that in the family recorded herein the mode of inheritance was a simple regular dominant.

7. Histologic study of one of the smallest papules showed that its site was periporal. A large lesion showed parakeratosis.

8. The nonfamilial and familial cases are inseparable except for probable differences in their genotypes. A nonfamilial case may also represent a mutant.

The following physicians examined members of the family studied: Bedford Shelmire, Dallas, Texas; J. R. Lowery, Salisbury, N. C.; R. G. Grose, Harmony, N. C.; Dewell Gann, Sr., Benton, Ark., and S. L. Segraves, Era, Texas.

1017 Medical Arts Building.

ROENTGEN RAYS IN THE TREATMENT OF ACNE

EVIDENCE THAT THEY DO NOT PRODUCE SCARRING

HENRY D. NILES, M.D.
NEW YORK

The rôle played by roentgen therapy in the occurrence of scars following the treatment of acne vulgaris by this agent has long been a disputed question. Every physician who has had experience in treating this disease with roentgen rays has repeatedly been forced to reassure many patients on this point because they have heard numerous, dire tales from friends about the unsightly scars thus produced. For a long time, it had been my opinion that this belief was limited to those outside the medical profession, but recently Dr. George Miller MacKee told me that it was also held by many physicians and a few outstanding dermatologists. At his suggestion, I have attempted to settle this question in the following manner:

In forty consecutive, unselected cases of acne vulgaris, seen in the dermatologic department of the New York Post-Graduate Hospital from Oct. 16, 1930, to June 1, 1931, one-fourth skin unit (one-fourth erythema dose, or approximately 70 roentgens) of unfiltered x-rays each week was directed to the right cheek and a placebo treatment to the left cheek. The latter was given by turning on the filament current but not the rays, pointing the target toward the ceiling or filtering the rays with several layers of heavy lead for the same length of time as for the actual irradiation on the right side, the patient thereby receiving no real treatment on the left side. The eyes, scalp and chest were shielded in the conventional manner. The factors for the exposure of the right cheek were as follows: 2 milliamperes $\times$ 125 kilovolts $\times$ forty-five seconds at a distance of 8 inches (20.3 cm.). The patients were observed after every four exposures, and the treatment was continued until the right side or both sides were well. The total number of treatments was from seven to sixteen; the average was twelve and one-half. The usual supportive measures, such as diet, treatment of constipation and dandruff and, when possible, removal of foci of infection, were carried out in every case. If lesions were present on the chest or back, these areas were treated in the regular manner. The cases were as follows:

Total no. of patients: 40 (female, 25; male, 15)
Average age: 21.2 years
Average duration: 4 years

From the Department of Dermatology and Syphilology, New York Post-Graduate Medical School and Hospital.

Read before the Section on Dermatology and Syphilology at the Eighty-Third Annual Session of the American Medical Association, New Orleans, May 13, 1932.

Location:	face only	25
	face and back	8
	face and chest	1
	face, back and chest	6
Description:	severe acne	16
	moderate acne	18
	mild acne	6

The average number of roentgen treatments was twelve and five-tenths. Before treatment the scars were equal on both sides in thirty-four, more marked on the left side in four and more marked on the right side in two. The lesions were equally severe on the two sides in thirty-five patients, more marked on the right side in four and more marked on the left side in one.

The results of treatment [1] were:

Both sides well and equal	13
Both sides almost well and equal	3
Both sides much improved and equal	3
Both sides slightly improved and equal	4
Right side well; left side almost well	6
Both sides improved, right more than left	2
Right side well; left not well	4
Neither side entirely well, but right better than left	2
Neither side entirely well, but left better than right	2
Not much change on either side	1
	40

Scars:	equal on both sides	32
	greater on left	5
	slightly greater on right	3
		40

Subsequent course:	remained well	11
	recurrence (severe)	3
	few lesions	9
	right side well; left not well	5
	no improvement	2
	patient did not return	10
		40

COMMENT

In his book on roentgen therapy, in the chapter on acne, MacKee [2] said: "It is the consensus of opinion that the best way to avoid scarring in severe cases of the disease is to check the affection as soon as possible,

1. The patients who received treatment on the chest and back obtained no better results than those in whom only the right side of the face was treated.

2. MacKee, G. M.: X-Rays and Radium in the Treatment of Diseases of the Skin, Philadelphia, Lea & Febiger, 1927, pp. 440 and 441 and figures 160, 161 and 162.

and x-rays are used for this purpose. Acne, no matter how treated, is likely to produce scars." He showed a photograph of active lesions and severe scarring due to acne in a patient who had not received roentgen treatment, and stated that most of this scarring could have been prevented by roentgen therapy. He also showed two pictures of the same patient, one showing severe scarring before roentgen treatment and the other, the absence of lesions but the same amount of scarring after twelve treatments with fractional dosages, and commented that "there would have been much less scarring if x-ray treatment had been used early in the disease."

In his lectures at the New York Post-Graduate Medical School, Dr. MacKee has repeatedly stated that in his thirty years' experience he has never seen acne scars made worse by roentgen rays, and that at times severe indurated acne may leave few scars while mild acne, consisting of a few papules and comedones, will leave numbers of small pits, regardless of the type of treatment. He regards this result as a matter of idiosyncrasy or a personal peculiarity.

In a further review of the literature, I could find no articles devoted solely to this subject but came across the following opinions expressed during the reading and discussion of papers on the results of roentgen treatment of acne vulgaris. Hazen and Eichenlaub [3] said:

> One of the most serious criticisms that have been made regarding the roentgen-ray treatment of acne is that it will produce deeper pits owing to the fact that the scar tissue is supposed to be absorbed by the rays. We have watched all our cases carefully and it is possible that in three instances the pits were deeper than they would otherwise have been, but we are not certain that this is true. As a matter of fact the amount of treatment given to an acne lesion would not have any influence on a hypertrophic scar, and it is rather difficult to see how the scar tissue in the acne lesion could be affected.

In the discussion of the aforementioned paper, Dr. Fred Wise [4] said:

> With regard to the pitting, that is more or less a psychologic matter. Many patients come in with pits due to the acne itself, and they are made more prominent by the disappearance of the acne lesions. From my experience, roentgenotherapy has no causal effect on this pitting, but when you clear up the acne, the pits which were there long before the acne was cured are more conspicuous, and the patients are dissatisfied when they see these blemishes.

Dr. William H. Guy [4] agreed with Dr. Wise, "that the pits that are seen and so frequently ascribed by patients to the roentgen ray can with better grace be credited to the disease itself." According to Dr. Pusey,[4] "In the badly indurated acne cases there is a destruction of the sebaceous glands of the skin by the roentgen rays, causing more pitting than would

3. Hazen, H. H., and Eichenlaub, F. J.: The Roentgen-Ray Treatment of Acne Vulgaris, Arch. Dermat. & Syph. **4**:671 (Nov.) 1921.

4. In discussion of Hazen and Eichenlaub.[2]

otherwise occur, but such patients do not mind a few pits." Dr. Ernest L. McEwen stated: "I think pitting in pustular acne as a result of roentgen ray treatment is analogous to the scarring which occurs in smallpox in that exposure to actinic rays is known to increase the degree of pitting and scar formation in the latter disease." He thought that pitting after x-ray was not merely a relative matter but in some cases more than one would expect after other treatment. Dr. J. C. Michael,[5] in a paper read at the fiftieth annual meeting of the American Dermatological Association, said " . . . scars are a natural consequence of the condition, and may be disregarded. A few patients complained of increase in the lanugo hairs in the irradiated areas, but I was never

Fig. 1.—No lesions are present on the right side but there are several on the left. Greater scarring is present on the left side after thirteen treatments with fractional x-rays on the right side only.

able to satisfy myself that this had really occurred." In discussing this paper, Dr. H. G. Irvine[6] said: "My own impression is that a greater amount of scarring does not follow the use of roentgenotherapy."

Even before starting this experiment, I had always felt that roentgen rays were not responsible for the bad scars which frequently remain after the cure of a severe case of acne, their apparent prominence being due to the absence of the disfiguring lesions which had previously

5. Michael, J. C.: Roentgen-Ray Treatment of Acne Vulgaris, Arch. Dermat. & Syph. **17**:604 (May) 1928.

6. Irvine, H. G., in discussion of Michael.[4]

engaged the patient's attention. I have seen some early cases of severe acne cured by roentgen rays, leaving no scars, while, on the other hand, some of the worst scarring that I have observed occurred in patients who received no treatment. The most unsightly pitting after any method of treatment resulted following repeated incision and drainage of the pustules. Except for the occasional factor of personal idiosyncrasy, the amount of scarring following acne usually varies directly as the severity and duration of the eruption, and the sooner any effective treatment is started the less scarring will result. In cases of equal severity cured by roentgen rays and by other methods, as a rule, I have found no difference in the amount of resultant scarring.

It was surprising and interesting to find in so many patients that the untreated side also improved and in some instances was cured as soon and as completely as the treated side. It was thought that this effect might have been caused by rays passing through the face. Dr. Cipollaro determined by an ionization dosimeter the number of roentgens reaching the untreated side. He found that with an exposure of 100 roentgens only 2 roentgens (one-fiftieth of the dose) passed through the face to the opposite side. According to this ratio, out of approximately 70 roentgens (one-fourth erythema dose) directed to the right side, only 1.4 roentgens would penetrate the face and reach the left side. Although this method measures only gamma rays, they are the only ones which need be considered, and the amount is negligible and far too small to produce any clinical effect. There are several other possible explanations of this unexpected improvement of the untreated side. It may be partly, or entirely, due to the beneficial effect of the general hygienic measures employed in each case. The disappearance of acne lesions without any local therapy is often seen after a change to a proper diet, the correction of constipation and the removal of foci of infection. One might assume some kind of sympathetic response, such as occurs when all the patches of psoriasis clear up after one patch is treated or when several warts disappear after only one has been destroyed. The effect may be psychic (the noise of the machine) or due to the flow of irradiated blood from the treated side. Desjardins [7] recently called attention to the exceptional radiosensitiveness of lymphocytes. He considers that the effect of roentgen therapy in inflammatory conditions is due to destruction of the surrounding zone of lymphocytes. It is possible that the number of these irradiated lymphocytes passing in the circulating blood from the treated to the untreated side was sufficient to produce the effects seen. One must also consider an indirect roentgen effect, namely, a foreign protein reaction from the destroyed cellular elements in the irradiated skin. Esophylaxis and the stimulation of

7. Desjardins, A. U.: Radiotherapy for Inflammatory Conditions, J. A. M. A. **96**:401 (Feb. 7) 1931.

Fig. 2.—Equal scarring and no lesions are present on either side after fourteen treatments with fractional x-rays on the right side only.

Fig. 3.—Equal scarring and several pustules are seen on both sides of the face after sixteen treatments with fractional x-rays on the right side only.

immune bodies must also be considered. By further experiments I shall endeavor to shed more light on this problem.

From the summary, it can be seen that the percentage of cures of the treated side (57.5 per cent) is considerably less than that usually obtained in the routine roentgen treatment of both sides of the face (at least 80 per cent). This may be partly explained by the fact that fewer rays reached the mesial part of the right side of the face, owing to the lack of overlapping irradiation from the left side. I feel, however, that another cause must be considered here, viz., the absence of the stimulating effect of the roentgen rays on the left side. The same unknown factor which, through exposure of the right side alone, caused improvement or cure of the untreated left side is absent in these cases, owing to the fact that the left side was not irradiated. This may be the cause of the unusually low percentage of cures of the treated side.

In spite of the opinion of many physicians and laymen that roentgen rays cause or increase the growth of hair on the face, in none of these patients could I detect any difference in the amount of hair on the treated and untreated side. As was to be expected in a condition such as acne, in which there is hypertrophy of the sebaceous glands, several of the patients before treatment presented an excessive growth of lanugo hairs, but this was no greater after than before treatment.

MacKee admitted that a growth of down is occasionally seen after roentgen treatment of acne, but stated that it is just as frequently seen in acne that has not been treated with roentgen rays. He brought out the fact that no one has noticed a growth of hair after roentgen treatment of other dermatoses, and he said that hypertrichosis following acne vulgaris is probably due to the disease itself, perhaps enhanced by the use of various stimulating remedies.

SUMMARY

1. In forty patients who were given an average of twelve and one-half weekly exposures of one-fourth skin unit of roentgen rays on one side of the face and a placebo treatment on the other, the scars were equal on both sides in thirty-two cases, more pronounced on the untreated side in five and greater on the treated side in three.

2. The amount of scarring after acne vulgaris depends on the severity and duration of the eruption and the tendency of the patient's skin toward scar formation. This seems to be neither increased nor decreased by roentgen therapy.

3. In nineteen of the forty patients, the untreated side was either entirely cured or almost well and as much improved as the treated side. Several theories as to the possible explanation of this unexpected finding are given.

114 East Fifty-Fourth Street.

ABSTRACT OF DISCUSSION

DR. JEFFREY C. MICHAEL, Houston, Texas: This is an extremely valuable and interesting paper—valuable from both the medical and medicolegal standpoints. Every one has had experience with the patient who attributes the scarring following roentgen treatment to the treatment and not to the disease. Often it is difficult to set these patients right. This paper furnishes a solid basis for one's explanation to the patient. Before treatment for acne is begun and several times during the treatment it is advisable to explain the nature of the scarring in acne and to make the patient understand that the roentgen rays do not produce the pits.

I agree with Dr. Niles that evacuation of pustules and comedones or any other minor procedure of that kind will increase scarring. There is, however, one complication of the roentgen treatment of acne which I believe causes more scarring than if that treatment is not used. I refer to the rare instances of explosive exacerbations of acne that follow the first few doses, sometimes even the first dose. These cases are not the ordinary mild exacerbations that are fairly common and of no special concern. In the cases that I have in mind the condition, unless judiciously handled, may eventually result in marked cystic formations and fistulous tracts which leave, as a final result, pronounced scarring. Teachers of postgraduate dermatologic students should emphasize this occurrence because I have seen two well trained dermatologists who did not realize what this explosive exacerbation meant.

An interesting feature of Dr. Niles' paper is his finding that the untreated side of the face showed about the same percentage of cures as the treated. He has had only forty cases, however, an insufficient number to come to any conclusions about, and the average age of his patients was 21 years, a period of life at which acne often disappears spontaneously. I believe that we should await a larger series before trying to explain these results. However, it recalls to mind the fact that there are no well worked up statistical studies of the results of the treatment of acne before the irradiation era, and therefore we are not in a position to compare statistically our present results with those of former times. We have only the statements of older dermatologists that their results were unsatisfactory.

DR. HOWARD FOX, New York: Dr. Niles has performed a useful service in discussing the possibility of scars being caused by x-rays in the treatment of acne. Many of our patients have this idea, especially when they see the rapid disappearance of acne lesions and notice scars in their place. While most dermatologists doubt that such scarring takes place, this is the first definite proof that we have had about the matter. It is comforting to hear Dr. Niles' results, and I hope that he will continue this work and report on a larger series of cases observed over a longer time.

DR. C. F. LEHMANN, San Antonio, Texas: I want to ask Dr. Niles to follow these patients, if possible, and report from three to five years from now. I think that this would be well worth doing, for the question will be brought up as to whether the greatest amount of scarring will not show up as a remote sequel.

DR. FRED D. WEIDMAN, Philadelphia: I do not use roentgen rays in the treatment of acne, but I can readily see how medicolegal complications might arise. I do not know whether this occurs often enough to justify routine photographs of the patient before treatment and after. That will, of course, have to be determined by the general dermatologic practitioner.

I am prompted to join this discussion only because in following the progress of keloids and the pitting in lupus erythematosus I found the application of plaster of paris to be a simple, time-saving and efficient way to keep track of the progress of elevations and depressions of the surface, and also to keep track of the pits. It gives the third dimension in a way that photographs may not. Dental plaster sets rapidly, and hardens in a minute and a half. In fact, one has to work rapidly to get the plaster in position before it becomes hard, but I can see how it would be a useful practice to place plaster over the face of patients with acne, label it and file it away. This would be a definite record of the condition of the skin in the beginning and at different stages during the treatment, if the physician chooses to repeat the process.

Dr. Clark W. Finnerud, Chicago: Did the lesions in any of these cases consist largely of comedones? From a practical standpoint—and I have run no careful tests such as Dr. Niles has—I have been under the impression that the cases which consist almost entirely of comedones and also those which exist largely in the form of deep suppurative lesions have shown an accentuated scarring following roentgen therapy as compared with the cases of that type in which other methods were used for a considerable period of time and were then followed by this therapy.

Dr. J. R. Allison, Columbia, S. C.: I was taught to give one-fourth dose of roentgen rays at weekly intervals for as many as sixteen consecutive treatments. I wonder what the opinion is today in regard to that form of treatment. I have long since stopped giving more than four consecutive treatments of one-fourth erythema dose each. I believe that more than this is harmful and will result in scarring.

I have heard a great many persons remark that the pustules should never be opened, that it increases the scarring. In the treatment of superficial acne with roentgen rays and strong lotions, they begin to localize in certain areas and the rest of the face clears up. I am of the opinion that these deep-seated pustules should be opened and drained. The tension and destruction of this pus causes deeper pitting than opening them with a small cataract knife.

I should like to hear Dr. MacKee express some opinion about the continued use of one-fourth erythema dose at weekly intervals.

Dr. W. J. Macdonald, Boston: We are all faced at times with the medicolegal problem. Therefore, it is right to disclose actual findings. Recent reports have shown the cure of acne vulgaris by means of roentgen rays given in eleven doses. Personally, I find that it requires about fifteen doses, when the MacKee technic is used. I find that roentgen therapy for acne sometimes, in the beginning, causes an exacerbation of the disease. This disappears as treatment progresses. I have not observed erythema following or during roentgen therapy. I believe scarring to be caused not by roentgen therapy but rather by the disease itself. General treatment and vaccines I find valueless in acne unless combined with roentgen therapy. Astringent lotions should be avoided during treatment. I believe that ultraviolet rays are valuable in mitigating the scars of acne. Dr. Andrews is in accord with this assertion, as stated in his recent textbook. I, therefore, support Dr. Niles' paper in stating that roentgen rays do not cause scarring in acne.

Dr. George M. MacKee, New York: Dr. Niles stated that the amount of roentgen rays administered would have no effect on hyperplastic tissue. While not an important part of the article, the statement is incorrect and should be altered.

The work carried out by Dr. Niles is important, especially from a medicolegal standpoint. In the patients treated by him there was no difference in the amount of scarring on the treated and untreated sides. This result is interesting and important, but not absolutely conclusive. It is possible that another series of cases will show a different result, although I doubt it. Theoretically, it is conceivable that roentgen rays, in some cases, may interfere with the formation of connective tissue, but it has always been my impression that roentgen rays do not increase the amount of scarring. There has never been any convincing evidence in favor of the opposite view. Dr. Niles has presented the first attempt to settle the controversy definitely, and thus far his work supports the belief that acne scars are not made worse by roentgen rays. This is probably so regardless of technic or dosage. The best way to prevent scars is to cure acne as quickly as possible, and roentgen therapy is one method of attaining this objective. Individual peculiarities play an important rôle in the production of scars. In some cases unsightly pits follow comedones and small superficial pustules, while in other patients a severe acne indurata is followed by little or no scarring—irrespective of the type of treatment administered. I have practiced dermatology for many years. I can say that in the past various types of treatment have been blamed for acne scars, and many legal actions have resulted from such erroneous opinions and beliefs.

A very small percentage of patients get worse during the first month or two of treatment. Whether this is or is not due to treatment is not definitely established. On the assumption that it is due to the treatment, a larger number of scars might result from the increased number of lesions. This phenomenon was not encountered in any of Dr. Niles' patients. I am not convinced that roentgen rays ever cause acne to exacerbate. I see similar exacerbations with other types of treatment and without treatment. Incidently, I see more and worse scars in patients with acne who have been neglected or treated with other methods than those treated with roentgen rays.

Our technic, while safe and sufficiently accurate for practical purposes, is not sufficiently accurate for scientific research. Technic is being improved. It is possible that in the near future we all can measure the dose of roentgen rays with a precision that will answer scientific requirements. Until that time arrives, a considerable discrepancy between the therapeutic results obtained by various clinicians must be expected and adequate allowance made.

Dr. Elmo D. French, Miami, Fla.: It has been my policy always to discontinue treatment during the menstrual week, because then a flare-up of the acne lesions always occurs.

Dr. Earl D. Osborne, Buffalo, N. Y.: I wish to mention one possible explanation for the clearing up of the untreated side. We have numerous evidences of the effect of the glands of internal secretion on the production of acne. It is primarily a disease of puberty, showing flare-ups during menstruation. I wish to offer the suggestion that the clearing of the untreated side may be due to the effect on the glands of internal secretion through the action of roentgen rays on the sebaceous glands. Following out this theory we began giving small doses of thyroid extract to some of these patients and were surprised at the number of patients in whom the condition cleared up. I think that this is a rational explanation for the clearing up of the untreated side, the effect on the thyroid gland.

Dr. E. R. Seale, Houston, Texas: I wish to stress again the marked pustular flare-up that one sees frequently following from one to four treatments with roentgen rays. I agree with Dr. Michael in that when this flare-up begins, roentgen therapy should be discontinued; otherwise large deep-seated lesions and later severe

scarring will result. It has been my observation that following the subsidence of the process the acne is usually cured and remains so.

Another point that I should like to mention is the influence that climate or geographic location has on acne. People frequently develop acne on coming to Houston who have never had it before, and it clears up when they leave, only to reappear on their return. So far as I can see, the only factors that can be blamed are the marked humidity, which naturally interferes with elimination of the skin, and the high iodine content of the foodstuffs.

Dr. William A. Rosenberg, Chicago: I should like to ask whether in this series the treatment was given with the standard roentgen unit, and whether the treatments were given every week in the entire series.

Dr. Henry D. Niles, New York: I agree with Dr. Michael as to the necessity of telling patients that scars are almost certain to appear. I tell them that the disease itself produces scars, that they should be prepared to see them and that the roentgen rays will not take them away. Of course, I realize that forty patients are not many, but it is difficult to get patients to cooperate. A number of the patients became aware of the fact that they were not getting any treatment on the left side of the face and they stopped coming. I think there were a hundred and eighteen patients in the group with which I started, but only forty were observed long enough to report on. I expect to go on with this work, using one-fourth unit on one side and a placebo on the other, and also double placebo treatments and other types of investigation and hope to report on it later.

Of course there is a spontaneous tendency for acne to clear up in young patients. Although I was interested in the scarring in the beginning, I became more interested in the clearing up of the other side. It almost made me change my ideas as to how the roentgen rays work. Presumably, the improvement is due to decrease in the activity of the sebaceous glands, but it seems to me there must be also some other factor.

Regarding Dr. Finnerud's remarks, I tried to be fair and not take into account the spontaneous disappearance of the very mild types.

There was no local treatment given these patients; nothing was used on the face except soap and water.

I found that most of the patients required from fourteen to sixteen treatments, but I should say that from 15 to 20 per cent can be cleared up with twelve treatments and a few with less.

Dr. MacKee mentioned the reference to the effect on hyperplastic scars. This was a quotation from the paper of Dr. Hazen and Dr. Eichenlaub.

As to the effect on the thyroid, a large lead protector was used that fitted closely under the chin and covered the patient to the shoulder on both sides, so I doubt if the thyroid received any radiation.

We gave one-fourth skin unit of roentgen rays every week, with very few exceptions. Perhaps one or two of the patients missed a week or two, but the majority of them had this amount every week.

EXPERIMENTAL MONOSPOROSIS

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AND
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The discouraging feature in the study of deep mycoses lies in the fact that one of Koch's requirements can but rarely be fulfilled: the reproduction of the disease in a suitable host. Even Koch [1] admitted that this point might be dispensed with under certain circumstances, yet in its absence every investigator feels that an important link in his chain of evidence is missing. Most fungi isolated from human mycoses prove to be entirely apathogen for laboratory animals. One group of these mycoses, the true mycetomas (Pinoy) or maduromycoses (madura foot), which is characterized by the presence of grains of various colors and produced by fungi with thick, septate, mycelial filaments, has been particularly difficult to transmit to animals.

Of all fungi isolated in the latter group, Monosporium apiospermum shows a fairly constant pathogenicity and the widest distribution. It was found to be the cause of maduromycosis in Italy by Tarozzi [2] (1909), by Radaeli [3] (1911) and by Pepere [4] (1913); in Brazil by Piedro S. de Magelhães [5] (1916), by Democrito Linhares [6] (1917) and

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1. Letter of Robert Koch to F. Neufeld (July 9, 1905); quoted by Neufeld, F.: Zum 25 jaehrigen Gedenktage der Entdeckung des Syphiliserregers, Deutsche med. Wchnschr. **56**:710 (April 25) 1931.

2. Tarozzi, G.: Ricerche anatomo-pathologiche, bacteriologiche e sperimentali sopra un caso di actinomicosi del piede, Arch. per le sc. med. **33**:553, 1909.

3. Radaeli, Francesco: Micosi del piede da Monosporium apiospermum, Sperimentale, Arch. di biol. **65**:383, 1911; Sulla monosporosi, ibid, **68**:268, 1914.

4. Pepere, A.: Micetoma a grani neri del piede, Sperimentale, Arch. di biol. (supp.) **67**:213, 1913; Sul fungo parasita di un micetoma a grani neri del piede (Carter) nostrana [Monosporium apiospermum, Sacc. (M. sclerotiale)], ibid. **68**:531, 1914.

5. de Magelhães, Piedro S.: Um caso de mycetoma podal de granulos brancos amarellados, Ann. do policlin. geral do Rio de Janeiro, no. 3, Dec., 1916. (Extracts from this article were furnished by Professor Brumpt [Paris].)

6. Linhares, Democrito: Sobre un caso de clinica cirurgica (mycetoma podal), Thèse de Rio de Janeiro, 1917.

by Fonseca and Arêa Leão [7] (1927); in Algiers by Montpellier and Gouillon [8] (1921), by Montpellier [9] (1924) and by Anderson [10] (1925); and in Paraguay by Delamare and Gatti.[11] In the United States it was reported by Gay and Bigelow [12] (1930), by Jones and Alden [13] (1931) and by Gellman and Gammel [14] (1932).

Radaeli,[3] Pepere [4] and, in 1923, Bolognesi [15] reported the production of granulomatous arthritis in animals by direct injection of Monosporium apiospermum and deemed intra-articular injection a particularly desirable method for the production of the disease in animals. Tarozzi [2] obtained positive results by intraperitoneal and subcutaneous injections which brought about the development of sclerotic, granulomatous nodules. In his later work, carried out in collaboration with Barbanti,[16] he called attention to the similarity in histologic changes produced by Monosporium apiospermum to those produced by other fungi. Radaeli [3] and Pepere [4] also transmitted the disease by inoculation into the anterior ocular chamber of rabbits. Gay and Bigelow [12] failed to produce any lesions in white mice and guinea-pigs. Viable cultures of Monosporium apiospermum injected by Jones and Alden [13] into various tissues of guinea-pigs and of a rabbit produced nothing but an inflammatory reaction in the eye of the rabbit, from which the fungus could not be recultivated.

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7. da Fonseca, O., and de Arêa Leão, A. E.: Scedosporium apiospermum, champignon producteur de mycétomes en Italie et au Brésil, Compt. rend. Soc. de biol. **97**:1347 (Nov. 18) 1927.

8. Montpellier, J., and Gouillon, P.: Mycétome du pied (type pied de Madura) dû à l'Aleurisma apiospermum, Bull. Soc. path. exot. **14**:285, 1921.

9. Montpellier, J.: Deuxième cas algérien de mycétome du pied (type pied de Madura) dû à l'Aleurisma apiospermum, Bull. Soc. path. exot. **17**:755, 1924.

10. Anderson, C.: Sur quatre nouvelles observations tunisiennes de mycétome, Arch. Inst. Pasteur de Tunis **14**:90, 1925.

11. Delamare, G., and Gatti, C.: Hyphomycète cultivable à grains blancs réniformes et durs (Indiella americana), Compt. rend. Acad. d. sc. **188**:1264 (May 6) 1929. The organism was later identified by Paul Peña as Monosporium apiospermum (Compt. rend. Soc. de biol. **104**:689, 1930).

12. Gay, Douglas M., and Bigelow, James B.: Madura Foot Due to Monosorium Apiospermum, Am. J. Path. **6**:325 (May) 1930.

13. Jones, Jack W., and Alden, Herbert S.: Maduromycotic Mycetoma (Madura Foot): Report of a Case Occurring in an American Negro, J. A. M. A. **96**:256 (Jan. 24) 1931.

14. Gellman, Moses, and Gammel, John A.: Madura Foot. A Third Case of Monosporosis in a Native American, Arch. Surg., to be published.

15. Bolognesi, Giuseppe: Micosi chirurgiche sperimentali, Pathologica **15**: 374, 1923; quoted in Bolognesi, Giuseppe, and Chiurco, Giorgio A.: Le micosi chirurgiche, Siena, Libreria editrice senese, 1928, vol. 3, p. 870.

16. Tarozzi, G., and Barbanti: Actinomicosi e Monosporosi, R. Accademia di scienze, lettere ed arti, Modena, sez. Sc., series 3a, vol. 12, 1915; quoted by Bolognesi and Chiurco (footnote 15).

When, therefore, one of us during the course of a mycologic study of a culture of Monosporium apiospermum succeeded in producing arthritis in rabbits with the fungus, it was decided to study the mechanism of the infection on a series of animals.

Monosporium apiospermum belongs to the Eumycetes, class Hyphomycetes or Fungi imperfecti, order Conidiosporales, suborder Sporophorineae, genus Monosporium, Saccardo,[17] 1911. This genus is characterized by spores on branched, decumbent conidiophores. Synonyms for Monosporium apiospermum are Scedosporium apiospermum, Scedosporium sclerotiale and Aleurisma apiospermum.

EXPERIMENTS

Monosporium apiospermum (Gellman and Gammel).—Intra-articular injections of a saline suspension of spores and hyphae were made into the knee joints of nine rabbits. One cubic centimeter of this suspension was injected lateral to, and just below, the patella, with the knee flexed. The suspensions were prepared by washing and macerating the surface growths of as many Sabouraud slants as were necessary to produce a uniformly turbid liquid. Cultures of the suspension were made at the time of injection to determine the viability of the organism.

The injections were made into both knee joints of six rabbits and into the right knee joint of the remaining three rabbits, and the animals were killed at varying periods after inoculation. In four there was no evidence of infection. In the five that developed arthritis the swelling of the affected joint was apparent within two weeks, and this was accompanied by increased local heat and by impaired locomotion. In two of the animals inoculated in both knees, only one joint was affected.

Complete autopsies were performed on all animals killed (except one, which was destroyed by mistake). Pathologic changes were found to be confined to the site or sites of inoculation, there being no metastatic lesions. Cultures of synovial exudate and of affected tissue were positive for Monosporium apiospermum in the five animals in which arthritis developed.

The rabbits in which arthritis developed were killed from eleven to two hundred days after inoculation.

The synovial sac was distended by thick, tenacious, gray fluid, and in the more advanced cases the fluid was purulent. In these instances small, dull-orange granules were present that proved on maceration to be masses of hyphae and spores. The synovia was thickened, and the synovial fat pads were indurated. Thirty-seven days or longer after inoculation, periarticular abscesses were encountered, some of which

17. Saccardo, P. A.: Sylloge fungorum omnium huiusque cognitorum, Padua, 1886-1906, vol. 22, p. 1287. Definition also in Gammel, John A.: The Etiology of Maduromycosis, Arch. Dermat. & Syph. **15**:241 (March) 1927.

communicated with the cavity of the joint, while others were closed. These contained thick, gray pus and varied as to the amount of surrounding fibrosis. In two animals there was destruction of bone and cartilage, which in one rabbit led to a spontaneous fracture of the femur. The bony invasion began in the end of the femur, just above the margin of the articular cartilage, with undermining and finally with solution of the cartilage.

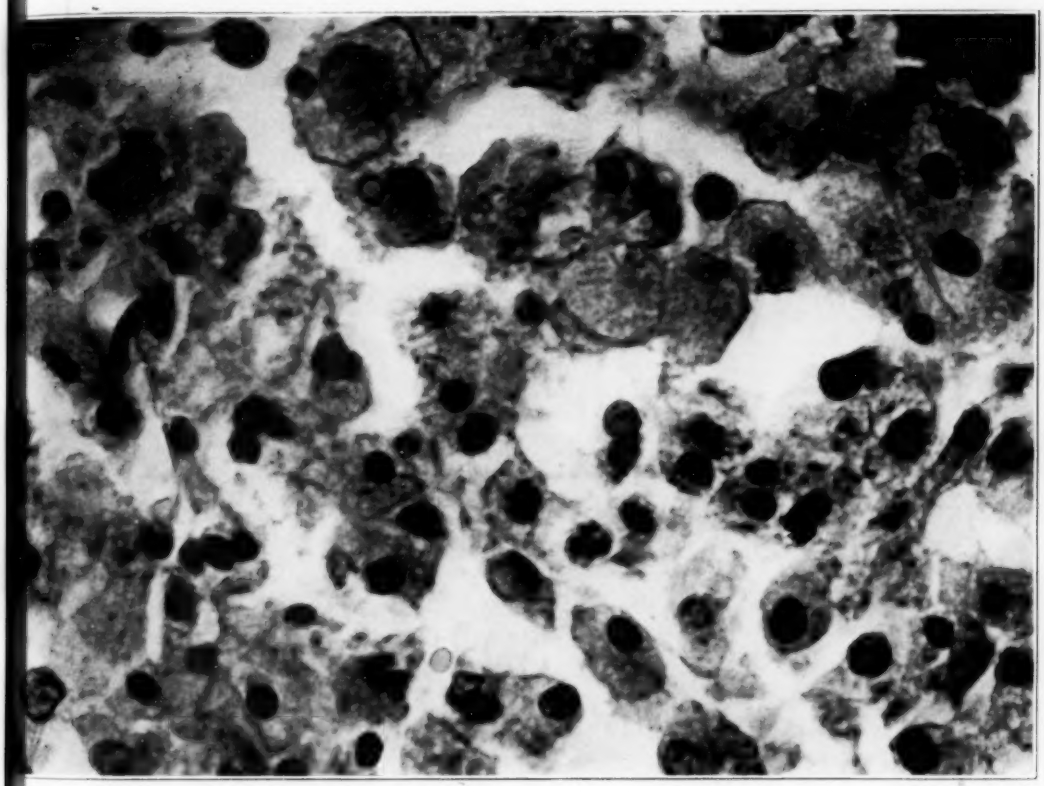

Fig. 1.—High magnification of peripheral zone of histiocytes, showing an intracellular spore; × 420.

Microscopic Examination: Within eleven days after inoculation there were proliferation and desquamation of the cells lining the synovial sac. The superficial cells were especially swollen, and there was no sharp distinction between the cells lining the sac and the deeper fibroblasts. There were multiple, small, necrotic foci, usually containing polymorphonuclear leukocytes in the superficial portion of the synovia. The soft tissue generally was edematous, hyperemic and infiltrated by endothelial cells, polymorphonuclear leukocytes and lymphocytes.

There were no qualitative differences between the lesions observed in the rabbit killed thirty-seven days after inoculation and those in the animals killed at later periods.

The abscess formation that in the killed animal at eleven days was limited to the synovia became extensive, with alteration and destruction of the periarticular soft tissue. The transitional stages between simple abscess formation and granuloma were gradual, and different stages could be seen in one animal. In general, the longer the survival after inoculation, the more fibrous and granulomatous were the lesions. Exudation remained a permanent feature of the inflammation and consisted of polymorphonuclear leukocytes, principally eosinophilic, endothelial cells and lymphocytes. The transformation from abscess to granuloma was accomplished by subcapsular proliferation of histiocytes, which, instead of organizing the contents of the abscess, remained as closely packed, large, round or polyhedral epithelioid cells, having an abundant amount of faintly acidophilic cytoplasm and large, dense nuclei (fig. 1). Interspersed with these cells were eosinophils, and between this zone of cells and the fibrous capsule were collections of lymphocytes. The central area of necrotic exudative cells was basophilic and granular and was gradually encroached on and replaced by the modified histiocytes that exhibited phagocytic activity for cellular débris. Large and small giant cells, usually of the foreign body type, were found characteristically at the edge of the necrotic center of the granuloma. Just as the abscesses were supplanted by granulomas, spontaneous healing of the granulomas was accomplished by peripheral, fibroblastic proliferation and organization of the zone of epithelioid cells.

Where the granulomatous character of the inflammation was well established there was marked fibrosis, while in the earlier lesions with extensive suppuration there were edema, hyperemia and myxomatous degeneration. Cartilage was destroyed by dissolution from the surface in the form of concave defects, with vesicular degeneration of underlying cells. The bony changes were similar to those in the soft tissue. The involvement of the bone began immediately beneath the articular cartilage on the shaft, with cortical and trabecular absorption, necrosis and exudation and development of granulomas similar to those already described. This process led to an undermining of the lateral margins of the joint cartilage.

Organisms: Spores were recognized both in tissue and in exudate. They were ovoid or globular, with an average diameter of about 12 microns. They were brown, pale in the center and darker at the periphery and remained unstained by the hematoxylin and eosin, brilliant cresyl blue and Gram methods. They were most numerous in areas of suppuration and were often seen within phagocytes (fig. 1). Irreg-

ularly shaped, bright, acidophilic granules, not exceeding 200 microns in diameter, were found in some of the granulomatous lesions (fig. 2). These were closely approximated by exudative cells, and short, mycelial prolongations extended out between the surrounding cells. Frequently the mycelial character of these granules could be recognized, and spores were commonly present.

Controls: Four rabbits received intra-articular injections of a killed suspension of Monosporium apiospermum and were killed two weeks, four weeks, six weeks and nine weeks, respectively, after injection.

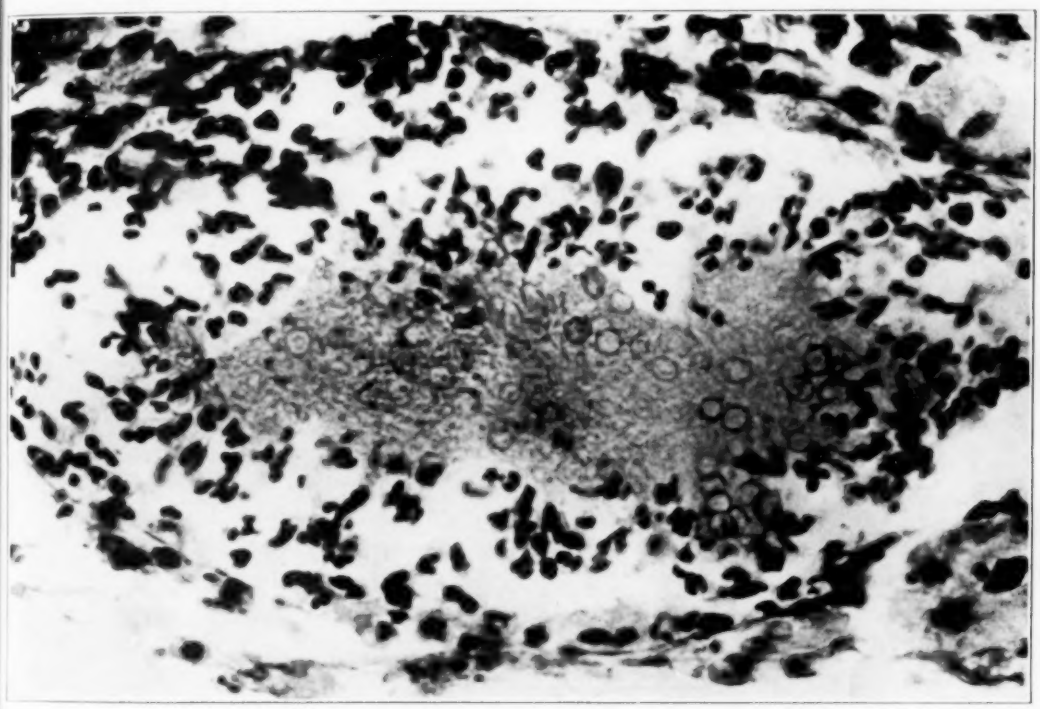

Fig. 2.—Small granulomatous lesion containing central granule in which there are many spores; reduced from a magnification of × 420.

In none of them were there synovial or periarticular changes comparable with those in the experimental series, nor was there any evidence of active inflammation.

Monosporium apiospermum (Gay and Bigelow).—Intra-articular injection was made into the knee joint of four rabbits with a saline suspension of spores and of hyphae from a culture of Monosporium apiospermum isolated by Gay and Bigelow from a case of madura foot. The rabbits were killed six weeks after inoculation, and in two of them granulomatous arthritis had developed, which extended into the peri-

articular soft tissue but did not affect the bone. The lesions were essentially similar to those described in the preceding series of animals. Cultures from the affected tissue were not positive.

Actinomyces asteroides (American Type Culture Collection).—Intra-articular injection of a saline suspension of the organisms was made in the same manner as in the preceding series of animals. Six rabbits were inoculated in both knees, and in two of the three rabbits in which arthritis developed, both knees were affected. One rabbit was killed at the end of thirty-nine days, and the other two in two hundred days after inoculation. The three rabbits in which no arthritis developed were killed two hundred days after inoculation. The lesions were similar to those produced by Monosporium apiospermum but accompanied by less suppuration and more direct formation of granulomas. The appearance of the fungus in the tissue differed in that there was no formation of spores, the caliber of the unseptate hyphal threads was not more than 1 micron, and the mycelial character of the granules was more uniformly recognizable. Cultures from exudate and tissue of these animals were negative.

SUMMARY

Cultures of Monosporium apiospermum obtained from two cases of maduromycosis of the foot in North America (Gellman and Gammel, Gay and Bigelow) were demonstrated to be pathogenic for rabbits by intra-articular injection into the knee joints. Spores and hyphae were recognized in the affected tissue and were in most instances recovered in pure cultures.

In seven of thirteen rabbits inoculated acute, and later chronic, arthritis developed, with involvement of synovia, cartilage, bone and periarticular soft tissue. In the earlier stages the inflammation was suppurative, and granulomatous lesions developed from abscesses. Abscesses and granulomas were commonly found in the same animal, and as older lesions healed, new ones developed.

A qualitatively similar arthritis was produced in rabbits by the injection of Actinomyces asteroides but could be distinguished by the appearance of the fungus in the tissue.

These experiments establish the pathogenicity of Monosporium apiospermum.

CHROMOBLASTOMYCOSIS IN TEXAS

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AND

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AND

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PHILADELPHIA

The blastomycosis with which North Americans are familiar is that due to a yeastlike fungus originally described by Gilchrist [1] which, long unnamed in formal botanic style, has been recently designated "Blastomycoides dermatitidis" by Castellani.[2] This organism produces a granulomatous, suppurative, chronic lesion which may effect both the skin and the internal organs. On the skin the condition is commonly verrucous and often resembles tuberculosis verrucosa cutis. Chromoblastomycosis, however, is essentially a South American disease. While it resembles North American blastomycosis in some ways, it differs from that condition in certain important respects. Thus, whereas both diseases are chronic and the cutaneous lesions may be most extensive, verrucous, crusted and malodorous, the internal organs do not appear to be affected in chromoblastomycosis; that is, metastasis has not been reported. The granulomas appear to be more superficial in chromoblastomycosis than in Gilchrist's disease, and in general chromoblastomycosis does not have the sinister possibilities of blastomycosis.

The most important difference, however, is the identity of the causative micro-organisms. In the tissues the fungus cell is dark brown; it does not produce true buds, and cultures made on standard mycologic mediums are black from the first. These features constitute a set of clearcut, final differential diagnostic criteria that effectually separate chromoblastomycosis from blastomycosis.

In South America, Acrotheca pedrosoi is the causative species. In North America, a similar organism appears to have been described once

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Read before the Section on Dermatology and Syphilology at the Eighty-Third Annual Session of the American Medical Association, New Orleans, May 11, 1932.

1. Gilchrist, T. C.: Johns Hopkins Hosp. Rep. **1**:269, 1896; Brit. M. J. **2**:1321, 1902.

2. Castellani, A.: Fungi and Fungus Diseases, Arch. Dermat. & Syph. **16**:714 (Dec.) 1927.

in connection with disease in human beings. Phialophora verrucosa Thaxter (Medlar,[3] 1915) was similarly dark brown in the giant cells and elsewhere in the cutaneous lesions of a man in Boston (Lane[4]). While the lesion did not in the least conform with South American chromoblastomycosis and the micro-organisms appeared to be likewise radically different, South American writers have adopted the case in their category, a procedure which seems to be justified in the light of the observations made in the case reported in this paper, in which the lesion was compatible with that in the Brazilian disease.

There are thus three geographic foci of chromoblastomycosis: Brazilian, Bostonian and Texan. Incidentally, the organism in none of these diseases reproduces by true budding. The organisms are not blastomycetes. The designation "chromoblastomycosis" does not connote either the biology or the classification of the etiologic agent, but only its brown color. The "blastomycosis" part of the nomenclature thus remains by sufferance, in deference to the South American practice of grouping different etiologic entities (blastomycosis, coccidioidal granuloma and even leishmaniasis are classified under blastomycosis[5]) in a common symptom complex and to the absence in medicine of standard rules of nomenclature for disease, such as are so firmly established in botany and zoology.

Dr. F. C. Mallory has lent us sections taken from the patient from Boston, and Dr. Olympio da Fonseca, of Rio de Janiero, has presented us with cultures and sections from patients with the Brazilian disease. Through the study of these sections, we have been able to compare the three diseases in the original materials.

REPORT OF CASE

History.—R. W. W., a man, aged 67, a farmer, first came under observation in August, 1931. He exhibited a polymorphous eruption on the right foot, which had begun as an ulcer on the dorsal side of the great toe forty years previously. After many months of treatment with local applications the ulcer apparently healed. On the site of the ulcer there developed a large wartlike lesion, and during the following years numerous other lesions developed over the entire foot and extended about 4 inches (10 cm.) above the ankle. At various times the foot was swollen and painful, and it itched intensely. During the ten years before he came under observation, the patient had suffered from one to four rigors a month, which were usually severe and accompanied by a high temperature of sufficient intensity to require the services of a physician.

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3. Medlar, E. M.: A Cutaneous Infection Caused by a New Fungus, Phialophora verrucosa, with a Study of the Fungus, J. M. Research **32**:507, 1915.

4. Lane, C. G.: A Cutaneous Disease Caused by a New Fungus (Phialophora verrucosa), J. Cutan. Dis. **33**:840, 1915.

5. da Fonseca, O., and de Arêa Leão, A. E.: The Chromoblastomycoses (English translation), Rev. med. cir. do Brasil **6**:23 (June) 1930.

Examination.—Examination disclosed an eruption consisting of warts, papules and nodules; the lesions were soft and fluctuant. The nodules were red or violaceous, and were covered with a layer of epidermis thinner than that on the adjacent skin. On puncture the nodules produced considerable hemorrhage. Some of the nodules had ruptured, forming ulcers with adherent crusts. The tissue found in the bottom of such ulcers was vegetative, and eventually produced verrucous lesions that grew higher than the surface of the healthy skin. Many of the lesions had fistulous openings from which exuded light amber-colored fluid, which hardened on exposure to the air. Adenopathy was absent.

The clinical appearance of the patient from Texas closely resembled that of the South American patients in the location and distribution of the lesions and in

Fig. 1.—Photograph of foot of patient taken in August, 1931.

the subjective symptoms, but the character of the lesions was somewhat different. This may be explained by the evolutionary characteristics of this disease entity.

Laboratory Data.—The blood count and the results of urinalysis were within the normal limits. The Wassermann and Kahn reactions of the blood were negative.

The small amounts of pus that could be expressed from a few of the sinuses were a dirty yellow and contained what grossly appeared to be granules of the same color, not unlike those of a ray fungus. However, microscopically, no organisms were recognized by direct examination of the hanging drop or by staining with any of the common stains (methylene blue, iodine or Gram's stain). Many saprophytic bacteria and large numbers of pus cells were seen. The causative organism was found, as will be indicated, by Dr. Weidman in biopsy sections (stained with hematoxylin and eosin).

Culture mediums of nutrient broth and agar, dextrose agar, Loeffler's blood serum agar and Sabouraud's sugar mediums were inoculated with the pus. The only successful culture was made on Sabouraud's medium, in which, at the end of the eighteenth day, there was noted a small, sooty-appearing, black colony. Subsequent laboratory studies and studies on animals were made from this culture.

To exclude tuberculosis, material from a lesion ground in a saline chloride solution was inoculated into the groin of a guinea-pig and injected intraperitoneally into two guinea-pigs. The first guinea-pig died at the end of four and one-half weeks with a large pyogenic abscess at the site of the injection. The other guinea-pigs gained in weight, and at the end of ten weeks autopsies were performed on them. No signs of a tuberculous infection or of chromoblastomycosis were found at the site of the inoculation or in the viscera in any of the three guinea-pigs. Corper's potato medium for growing tubercle bacilli was also inoculated into the animals; however, a growth could not be obtained.

A saline suspension of the fungus taken from the culture was injected intraperitoneally into another guinea-pig. This pig also gained in weight, and at the end of ten weeks an autopsy was performed. No signs of the disease were found. A similar suspension was injected into the groin of a white rat. The rat was very sick for several days, and a lump developed at the site of the injection. However, the rat improved, and later, at autopsy, only scar tissue in the groin was found.

HISTOPATHOLOGY

Materials from an older and a younger lesion were studied. Except for differences in the degree of epidermal hyperplasia (which was more marked in the older lesion), the histopathologic appearances were the same in the two. The interpapillary pegs were markedly broadened and elongated (acanthotic), owing to marked hyperplasia and swelling of the epidermal cells. Polymorphonuclears were frequently found infiltrating between the latter. The irregularity and elongation of the interpapillary pegs were never of the extreme, pseudoepitheliomatous type that is frequently observed in Gilchrist's disease.

The characteristic changes of the disease were found in the corium. The edema was extreme (less so in the older lesion). The granulomatous features extended from the papillae to the subcutaneous tissue, without a predilection for any particular level. For the most part, they consisted of a rather sparse infiltration of lymphoid and plasma cells among which giant cells of both the foreign body type and the Langhans type were scattered. Eosinophils and Russell's fuchsin bodies were numerous. Sometimes the giant cells were grouped, but in the absence of endothelioid cells the appearances were not at all those of tuberculosis or syphilis. Except for the presence of the fungous cells, the recessiveness of the endothelioid cells was the most important histologic differential diagnostic point for this disease. Incidentally, this type of change—essentially a foreign body reaction—can also be produced by other species of fungus such as Aspergillus. To such simpler types of reaction, additional features were added in places. Thus, areas of polymorphonuclears or sharply outlined foci of endothelioid cells often

occurred. In the latter cases, the picture was indistinguishable from that of tuberculosis, except for the presence of the specific micro-organisms. Miliary abscesses occurred in all levels of the corium, and when located at the tips of the papillae and sectioned in the appropriate plane they gave the effect of being intra-epidermal.

In substance, the picture was thus similar to that of tuberculosis, though often differing from it by reason of the miliary abscesses and

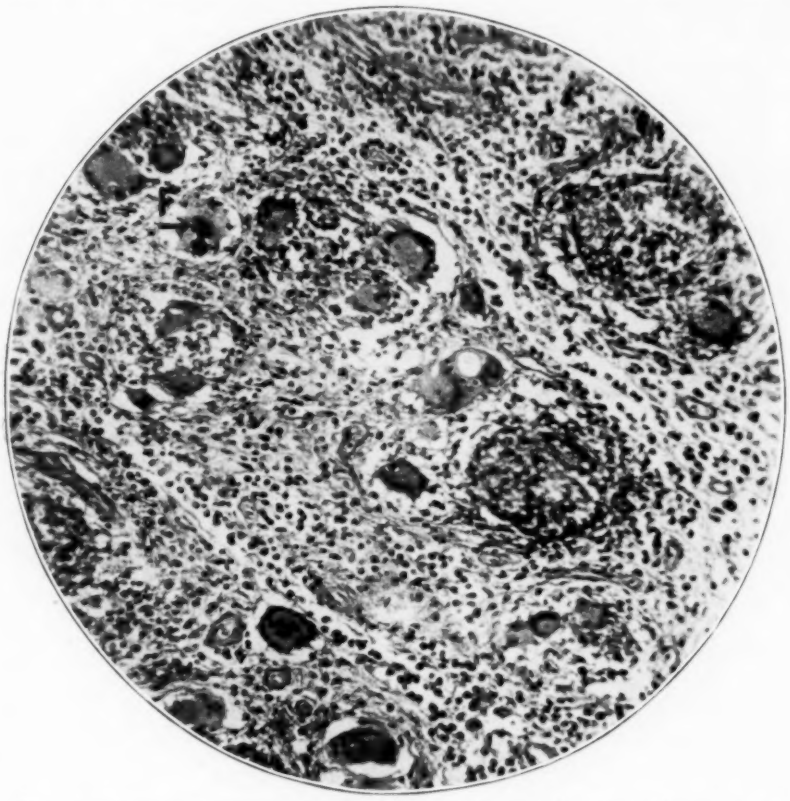

Fig. 2.—Chromoblastomycosis; granuloma (human tissue) with many giant cells. There is a cluster of fungus cells at *F*. These cells are dark brown.

by the associated foreign body reactions in which endothelioid cells were absent. The picture was unlike that in Gilchrist's disease in the absence of pseudo-epitheliomatous hyperplasia, but one can understand that a lesion which was old enough might be sufficiently papilliferous to give this picture. In any event, it is conceivable that the histology of chromoblastomycosis and that of Gilchrist's disease could merge to such an extent that only the differences in the specific micro-organisms would serve to differentiate them.

Comparison with Boston Case.—The granulomas in this case were confined to the papillary and the subpapillary regions. However, this superficial position may have been only an expression of the age and progress of the lesion; the duration was only one year, and the lesion was only 2.5 cm. in diameter. The predominant cell reaction in this case was tuberculoid. It was necessary to conduct searches before finding the foreign body type of reaction. This was just the reverse of

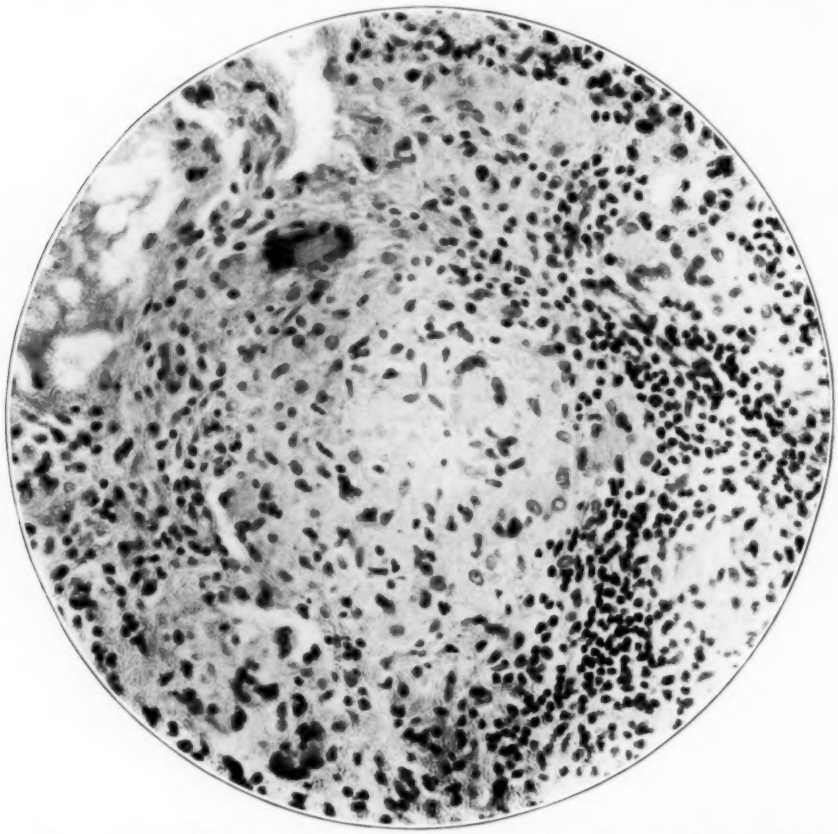

Fig. 3.—Granuloma resembling tuberculosis seen in a section taken from the testis of a white rat.

the Texan case. Plasma cells predominated in many of the lesions of the patient from Boston.

Comparison with Brazilian Disease.—In the Brazilian disease, again, the granulomas were confined to the upper parts of the corium. The order of granulomatous changes in the Brazilian patient was almost identical with that of the Texan. The epidermal hyperplasia was extreme; even in histologic sections it could be made out that the

lesion was highly papilliferous. Interpapillary pegs extended deeply and irregularly into the corium.

Histologic Summary.—Considering the three diseases collectively, it appears that the reaction to this high fungus form is of three types. The lowest order is that of a foreign body granuloma; the second is a tuberculoid reaction, and the third, an abscess formation. It is worth while speculating as to what extent these differences may depend on the virulence of the different cell forms which these higher species of fungus are so prone to develop. For instance, in nature or in the test tube, even a single cell colony will develop such different forms as conidia, phialophores and mycelial cells. In tissue it is understandable that the urge to produce different cell forms still persists, although it is not highly successful in doing so. In Bostonian chromoblastomycosis, Medlar saw approaches to mycelium formation (at least chains of cells), in view of which it is conceivable that physiologic differences, including virulence, would also obtain. Under such circumstances, together with the rôle which allergy and "constitutionalism" must play in determining the reaction of the tissue, we feel that attempts should not be made to differentiate these different forms of chromoblastomycosis on the basis of finer variations in histology such as Rocha Lima [6] and Gans [7] postulated. Certainly, the depth of the process in the corium should not be invoked without larger statistical material. The tubercle bacillus, for instance, can induce both most superficial and extremely deep lesions.

MYCOLOGIC STUDIES

Forms of Fungus in Tissue.—There is close similarity between the Brazilian, Texan and Bostonian forms. We have had the good fortune to study original materials in histologic sections, which were confined, however, to only a single case of each of the three types. The cells were largest and most numerous in the Brazilian disease, next in the Texan, and smallest and least numerous in the Bostonian. All were dark brown, and did not show true budding. According to the illustrations, the tendency toward chain formation was apparently most marked in the Bostonian case, although the appropriate specimens did not appear in the limited number of sections (three) available for our study. Transverse fission appeared in all three sections. Dr. F. C. Mallory, of Boston, presented us with other sections sent to him from the tropics, in which mycelium formation occurred on the surface of the lesion but not in the deeper parts; however, in the latter position, only the rounded forms were exhibited. The fission or septated forms

6. Rocha Lima: Arch. f. Dermat. u. Syph. **145**:312, 1914.

7. Gans, O.: Histopathologie der Krankheiten, Berlin, Julius Springer, 1928, vol. 2, p. 94.

in tissue are the strongest indications of a relationship with the multicellular aggregations comprising the sclerotia of Alternaria, Macrosporium and other fungi.

In lesions of rats, the fungus cells were of the smaller, slenderer type met in culture, rather than the coarser, more sclerotic type occurring in the Texan patient. However, they compared favorably with those in the Bostonian subject. This fact may be a commentary on the extent to which individuals may influence the morphology of a single fungus species, and may indicate that lines must not be drawn too sharply in the differential diagnosis of specific fungus cells in tissue.

Cultures.—The primary culture was secured by planting and selecting for further study whatever black fungus colonies developed.

On Sabouraud's conservation medium, growth was limited; colonies did not exceed 4 or 5 mm. in diameter even when four months old. They were slaty to coal black, and extended abruptly upward from the substrate to a distance of 3 or 4 mm. The margin was sharp. The colonies did not extend deeply into the medium; in fact, they were so lightly attached that there was danger of shaking them off by rough handling.

On dextrose agar (Pennsylvania medium [8]) the appearances were similar, except that growth was much more luxuriant. In three weeks colonies measured 2.5 cm. in diameter (in potato tubes measuring 15 by 2.5 cm.). The surface was lumpy, with suggestions of a circumferential arrangement of the nodulations. In colonies four months old, dissociation was indicated by the presence of an additional growth of fungus on top of the original one, which was softly fuzzy and pale brownish gray, and did not exhibit the nodular surface. The dissociative portions were not as hard and compact as the original colony. The underlying medium was not discolored black. The dark color indicated in the photograph was due to drying out.

Hanging Drop Culture (Twelve Days Old).—The mycelium was mostly of a beaded type, like that seen in mycoderma. The segments were short, measuring up to 3 microns in diameter; they tended to become rounded into spheroids, but they remained closely attached to each other. There were not any budding forms to suggest oidium. All fungus substance was diffusely pale brown; definite granules were never exhibited.

The special forms of differential diagnostic value were the phialides and the globi of conidia at their tips. These were barely distinguishable under the low power lens of the microscope; oil immersion studies were necessary in order to identify the details of the cup and conidial

8. Weidman, F. D., and Spring, D.: Comparison of Ringworm Culture Ingredients: II and III, Arch. Dermat. & Syph. **18**:829 (Dec.) 1928.

relationships at the terminus. These details, such as Medlar has described, could be easily overlooked in the absence of these precautions. The phialide most commonly extended laterally from a hypha but was frequently terminal. It measured 8 by 2.5 microns. Sometimes it was surmounted by a solitary minute conidium, but generally a minute cup surmounted the phialide. The cup was generally empty, owing to the facility with which the conidia escaped from it, in which case it could be mistaken for paired septums. When retained, however, the cup contained a minute globus of protoplasmic substance (gloea) enclosing small numbers (twelve to sixteen) of minute ellipsoid conidia.

The conidia had smooth surfaces, measured 2 to 2.5 microns in length and from 1 to 1.5 microns in width, and were colorless and

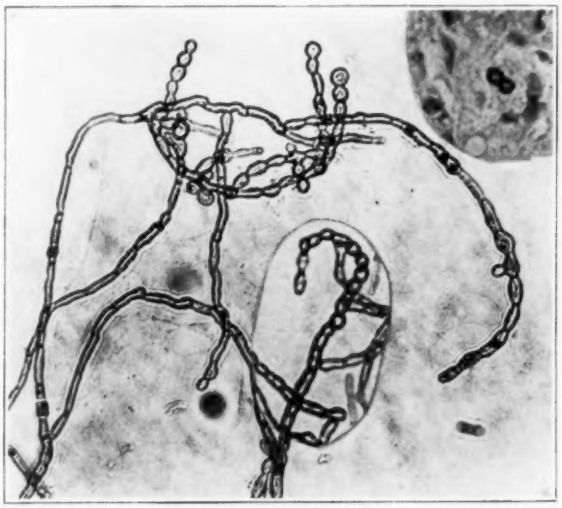

Fig. 4.—Hanging drop culture, showing terminal filaments moniliform. Insert in corner shows a giant cell from experimentally infected rat. The fungus cell shown is of the same magnification as the culture.

structureless. They collected in great quantities at the sides of mycelial filaments, giving an erroneous impression that they might be springing from them.

Forms were not found in culture similar to those seen in tissue, but this is not inconsistent with experiences met with in many other species of fungi.

Histologic Sections of Cultures.—Histologic sections of four months old dextrose agar cultures did not bring out additional features, such as sclerotium or ascus formation. Appearances were the same in principle as those described previously for the hanging drop.

Alternarial Forms.—A culture of Alternaria was recovered by retroculture from one of the white rats experimentally inoculated. We do not emphasize this observation because further studies would be necessary to show that this form was not a contaminant from the intestinal tract of the animal, but we feel compelled to record it because pseudo-budding forms which were almost identical with ones found in human tissue occurred in the hanging drop cultures.

Classification.—The character of the conidiophores, the subterminal cups and the terminal globi of conidia which have already been described

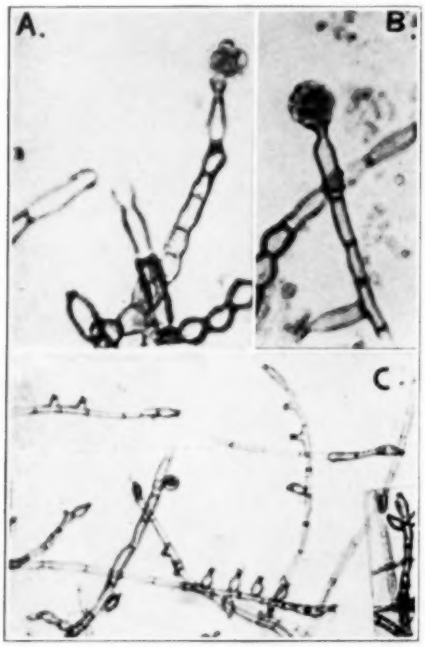

Fig. 5.—Hanging drop culture four months old, showing lateral and terminal phialides. *A* and *B* have been magnified 1,000 times (oil immersion) and *C*, 250 times. The globus of the conidia is still in situ in *A* and *B;* the conidia have become detached in the groups below. The clustering is suggestive of Sporotrichum groupings which are shown in the lower right hand corner.

at once reconciled the species with Phialophora verrucosa Thaxter (1915). All that it is necessary to discuss is the relationship of this species with the Brazilian fungus of chromoblastomycosis, Acrotheca pedrosoi.

On the basis of form genera, the two species are distinct, as the phialiform complex exhibited in P. verrucosa has not been described in the Brazilian species. We did not see the "knotted stick" forms emphasized by da Fonseca and Area Leao, or disjunctors. In other respects, however, there were close similarities, such as the approaches

to moniliform, cladosporium, hormodendrum and other arrangements of mycelium. It is evident that there is considerable variation in the mycelial architecture of the different strains which cause the Brazilian disease, as is indicated by the debate as to its exact position in botanic classification. Details may be found in da Fonseca and Area Leao's paper; the latter cited Langeron's [9] opinion that the causative fungus belongs in the genus Trichosporium and reproduced illustrations of Hormodendrum formations. However, we do not have the materials and perspective to pass on this controversy; we are concerned with it only so far as P. verrucosa may be related to Acrotheca pedrosoi. This relationship could obtain only under the hypothesis that they are form genera of a common genetic entity among the higher types of fungus.

The subject of form genera must be introduced here, because it is conceded that members of the fungi imperfecti, to which the two species discussed belong, have a life cycle. If, now, the appropriate conditions of environment and genetics could be secured, the form genus could become more complex and be made to appear in its more distinctive, significant and sexually classifiable botanic expression. The diagnosis of Acrotheca, Phialophora and other genera is therefore made on the basis of morphology, and not in the sense that each of such genera (or for that matter, families and higher groups) are valid genetic entities. Viewed in this broader light, it is altogether possible that Acrotheca and Phialophora represent different stages of one and the same species or genera. It is for this reason that the appearance of an Alternaria (also one of the fungi imperfecti) which we cultured from one of the lesions in a rat was not dismissed from consideration in connection with Phialophora verrucosa, particularly since the dark brown or black color of both appeared to relate them to the Dematiaceae. The appearances of pseudo-budding forms in the culture of this Alternaria which were similar to ones seen in the tissue from the Texan case is further in point. Although the evidence at present is weak, it is proper to suspect that both Phialophora and Acrotheca could be form genera of one of the Dematiaceae which occur so commonly on plant forms of the outside world, such as Alternaria and Hormodendrum. It is of further significance that almost all cases of chromoblastomycosis have originated from agricultural sections, if not actually in farmers, and that thorn punctures have been mentioned as the beginnings of the lesion.

ANIMAL INOCULATION

A thick emulsion from an old dextrose agar culture served as the inoculum. In rats 116, 117 and 118, a culture freshly isolated from rat 113 was employed as a test for virulence increased by passage.

9. Langeron, M.: Trichosporium Pedrosoi, the Cause of Brazilian Verrucous Dermatitis, Ann. de parasitol. **7**:145 (March 1) 1929.

Injections were made intraperitoneally, intratesticularly and, in some cases, into the deep tissues of the leg.

Mice.—One of two mice inoculated died and was largely eaten by cagemates. The second mouse exhibited only a few small nodules in the great omentum.

Rats.—Nine rats received injections. In no case did lesions develop in the leg or definitely within the viscera. Nodules occurred in only one or two cases on the surfaces of the spleen and liver, and they extended into the parenchyma for only short distances.

The prevertebral, mesenteric and inguinal lymph nodes were frequently involved by granulomas, and the great omentum almost invariably contained lesions. The skin became infected in only one case,

Table Showing the Results of Intraperitoneal and Intratesticular Inoculations Into Rats

	Injections	Testis	Great Omentum	Liver	Spleen	Regional Lymph Nodes	Retroculture
107	1	+	+	?	..	..	— (alternaria and aspergillus)
108*	3	+	..	..	..	..	..
112	1	+	+	..	..	..	..
113	1	+	+	..	..	..	+
114*	2	+	..	+	+	+	..
115*	2	+	+‡	..	..	..	..
116*	3†	(Animal largely eaten)		..	..	+	..
117*	3†	+	..	+	..	+	..
118*	3†	+	..	..	..	+	..

* This rat died spontaneously; the others were killed.
† One of the injections was made with a fresh strain from rat 113.
‡ Massive sarcoma of liver contained fungus cells.

that is, around a needle puncture. However, microscopic examination showed the histologic features of an abscess; it appeared that the fungus had not proliferated in the tissues. Certainly it had not excited granuloma formation as in other parts of the body.

Lesions developed consistently in the testes, inducing at times lesions two or three times the size of the normal organ. In two instances, the overlying skin exhibited sinuses leading from the testis.

Details are indicated in the table.

Comment.—The three rats inoculated with the strain from rat 113 died, with extreme emaciation; the others were only moderately emaciated. The organism did not appear to have ability to invade tissues deeply; evidently they did not metastasize by the blood. It was carried regularly to regional lymph nodes or deposited in the serosa of the liver, spleen and other portions of the peritoneal cavity, sometimes extensively. Since the material had been injected in quantities, the lesions were coal black, but as retrocultures were successful only

once, it appears that most of the organisms died. Passage increased the virulence to a slight extent, as judged by the greater emaciation of the animals and the somewhat larger size of the lesions.

PORTAL OF ENTRY

The most likely portal is the direct one, that is, from the exterior, since the disease is superficial; furthermore, the habitat of the fungus in rats is so precarious that it is not likely to survive passage through the interior of man. It should not be overlooked that the fungus may be a "secondary" possibility in the case; that is, that some preliminary defect of the skin such as tuberculosis (or the associated leishmaniosis reported in one of da Fonseca and Areo Leao's communications) is essential or contributory. Indeed, most cases of chromoblastomycosis have been regarded at first as tuberculosis verrucosa cutis until histologic examination has brought the fungus into the picture. It is particularly incumbent on one to remember this fact in view of the comparatively low order of invasiveness possible for fungi in general, although the Boston case at least was an exception, because Lane recognized certain clinical features that were indications against tuberculosis verrucosa cutis, and Medlar excluded the tubercle bacillus at least so far as staining tests would permit. We feel, however, that it is still necessary to attempt to exclude other diseases as associates, as the opportunity arises, before finally concluding that the fungus is not a mere contaminant, perhaps a foreign body. We have seen, for instance, foreign body reactions in the granulation tissue of ulcerated mammary carcinomas which were eventually found to be referable to strands of cotton fibers that had been sequestered from dressings. Dr. Kenneth M. Lynch has shown us granulomatous changes around a surgically extirpated appendix; lycopodium cells (dusting powder from surgeons' gloves?) appeared in the giant cells. Nevertheless, once in the tissues, the action of the fungus cells in chromoblastomycosis was more than that of simply a foreign body, since they showed clear evidence of reproduction and multiplication in tissue, and because the cells were located in the centers of both endothelioid and polymorphonuclear accumulations. This was so in both human tissue and in rat tissue.

It is still theoretically possible that this disease has an internal portal of entry. We have encountered sclerotic cells of a similar appearance within giant cells in the mesenteric lymph nodes removed at necropsy in a case of Kaposi's sarcoma. This is likewise a condition in which the legs become hyperkeratotic and verrucous, without, however, exhibiting granulomatous changes. Indeed, it would be compatible with present day tendencies to elaborate the scope of the mycids and to regard Kaposi's sarcoma as a cutaneous "id" with a primary

focus in mesenteric lymph nodes, or, perhaps, elsewhere if the presence of such fungi could be established with any regularity in internal positions. There is a basis for such theorizing in the report that fungi can be demonstrated in 10 per cent of all mesenteric lymph nodes at necropsy. Such a concept would also permit the metastasis of fungi from this internal position to the skin, resulting in lupus vulgaris-like lesions such as Lane described in Boston.

The South Americans are in a particularly advantageous position to inquire into the presence of Acrotheca pedrosoi in mesenteric lymph nodes. Indeed, exploratory laparotomy and biopsy might be justified in the graver examples of this condition, as well as in Kaposi's sarcoma in which the outlook is so serious.

SUMMARY AND CONCLUSIONS

An extensive verrucous disease of one leg, of forty years' duration, in a patient from Texas, was found referable to a fungus Phialophora verrucosa. This is the second authenticated case reported in the literature. The disease closely resembles tuberculosis verrucosa cutis and Gilchrist's blastomycosis. Histologically, it also resembles Gilchrist's blastomycetic dermatitis except that the microorganisms do not bud and are deep brown.

Phialophora verrucosa was isolated in culture. Injected into white rats, it almost invariably induced granulomas and injected into the testis, caseation. The organism was of extremely low virulence; it appears to be incapable of existing in the viscera or other deep tissues. Experimentally induced lesions remained localized at the sites of lodgment.

The histology of the Brazilian, Bostonian and Texan lesions was compared in the original materials sent from those places. In tissue the micro-organisms appeared to be identical. In view of the recovery of an Alternaria from one of the experimental rats, it is theoretically possible that the organisms from all three places are genetically the same, although not identical in culture.[10]

ABSTRACT OF DISCUSSION

DR. CLARK W. FINNERUD, Chicago: This extremely interesting paper should impress us with the importance of making a culture in instances of disease of the skin in which a definite diagnosis cannot otherwise be made. Merely clinical and histologic study alone frequently will not suffice, as is evidenced by the fact that in mycotic diseases there may be a noncharacteristic histologic picture, and it also may be difficult or impossible to demonstrate the causative organisms in the sec-

10. Cultures of Phialophora verrucosa are deposited at the National Collection of Type Cultures, London, and the American Type Culture Collection, Chicago (no. 4806). Histologic sections are on deposit at the Laboratory of Dermatological Research (D. R. 2,261), and the Army Medical Museum.

tions. A resort to cultural studies in such instances gives the only hope for verifying or rejecting the clinical diagnosis. We can all make the cultures, and there is always a Weidman to resort to for classification and interpretation of our observations.

When such methods are employed more as a routine measure we may find that chromoblastomycosis, as described by the authors and others, is not the extremely rare disease which it is now considered to be. It is possible that many reported and unreported cases which have been considered tuberculosis verrucosa cutis, blastomycosis and even coccidioidal granuloma, Madura foot and other disorders have, in reality, been instances of this particular disease.

It is unfortunate that chromoblastomycosis is so named, and I should suggest a revision by the authors in that it lends some confusion to the well known and well defined blastomycosis entity. As brought out by the authors, the name becomes unjustified by the fact that the apparently causative organism is not Blastomyces, as well as by the fact that the clinical resemblances to blastomycosis are not particularly marked, chromoblastomycosis being a superficial and probably never a systemic invader.

The old question arises as to whether or not the isolated fungus, because of its relatively low pathogenicity, is the true etiologic agent of this disease. Only further study can settle this point, although, in the light of the evidence presented, there can be little doubt of it in the cases here discussed.

The complete study of this case, of which only an abstract has been given, is a classic piece of scientific work and one which should be an inspiration to all.

Dr. C. Guy Lane, Boston: It is interesting to me to hear the presentation of another case of this type of infection. The patient, whom I saw originally in 1914 or 1915, had only two lesions. One lesion was open and the other was a rounded, nonulcerated nodule which, so far as I could find out, had never had a discharge. The ulcerated lesion was excised first, and the organisms were found. It was a question whether or not there was a contamination. Then the other lesion which was intact was excised and studied further, and we came to the conclusion that the fungus was probably the active infective agent. The cultures were studied with Professor Thaxter at Harvard, and it was at his suggestion that the name Phialophora was adopted. No other lesions appeared. The patient was followed for some time, but no other lesions developed.

As Dr. Finnerud has already stated, this case emphasizes the need for study of unusual organisms of this type, the need for culture and the need for examinations of smears and probably study with a competent mycologist.

Dr. Fred D. Weidman, Philadelphia: The differences between cases such as those which the authors have outlined are more those of the organism concerned than of the clinical appearance. Indeed, only when the micro-organism is identified culturally can one say how it should be classified; significant differences in tissue can scarcely be postulated.

The mode of division of the parasite in tissue is not by budding as in North American blastomycosis. It is not a true budding; in no place can a connection between the interior of the daughter parasite and of the mother parasite be distinguished.

It was necessary to carry out all of Koch's postulates in connection with this work, because black fungi such as these are such frequent laboratory tramps. Furthermore, they are ubiquitous on vegetation and might well be only symbionts to some other pathogen in the patient's skin. However, in the experimental work on the rat granulomas frequently developed in the testis, and the micro-organisms were found in the giant cells.

The features of most value in the final identification of the Texan organism is the flasklike factor surmounted by a little cup found sticking out from the sides of the hyphae as well as at the terminations. In the little cup there is a globus within which the conidia are embedded. It requires close microscopic study with a high power lens to make out these details. They are easily overlooked.

As I see it, the highlight of this presentation is that we have here one more of the bothersome clinical cases which is pigeon-holed as a granuloma of an indeterminate nature and which is frequently presented as such before all dermatologic societies; but, unlike other such cases, the identity of the causative organism has been established for Dr. Wilson's patient. Furthermore, it is a satisfaction to learn that improvement has been brought about by the use of iodides in a case which would ordinarily have been diagnosed as tuberculosis and in which, of course, the patient would have been denied the advantage of iodide therapy.

I did not see the patient, but Dr. Wilson informs me that there were no metastases. In the Brazilian cases metastases were not reported.

News and Comment

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

At the 1931 meeting of the American Dermatological Association, a committee was appointed to determine the advisability of forming an American board for the certification of competent practitioners in our specialty, similar to boards created by the ophthalmologists, the otolaryngologists and the obstetricians and gynecologists. A similar committee was appointed by the Section on Dermatology and Syphilology of the American Medical Association at its meeting in the same year. A favorable report was rendered by each committee at the 1932 meeting of each of the aforementioned organizations, and on May 11, 1932, the first meeting of the Board was held in New Orleans. On November 25 the Board was formally incorporated with the following members: Dr. Howard Fox, New York, president; Dr. William H. Mook, St. Louis, vice-president; Dr. C. Guy Lane, Boston, secretary; Dr. George M. MacKee, New York, treasurer; Dr. Harold N. Cole, Cleveland; Dr. Howard Morrow, San Francisco; Dr. Jay F. Schamberg, Philadelphia, and Dr. Arthur W. Stillians, Chicago.

The primary purpose of the Board is to determine the competence of physicians who specialize in dermatology and syphilology. It will prescribe certain standards of fitness, conduct examinations to determine such fitness and issue certificates to those who successfully fulfil the necessary requirements.

A second object is to publish lists of physicians who shall have been certified by the Board, for the benefit of hospitals, medical schools, other physicians and the lay public.

A third object is to improve the standards of practice of dermatology and syphilology by investigation of medical school curriculums and by investigation and encouragement of adequate facilities for graduate instruction in this specialty.

There are certain fundamental requirements for all who apply for certification. The applicant must be of high ethical and professional standing, a graduate of a medical school which is satisfactory to the Board and a duly licensed physician. Furthermore, the applicant must have received adequate training in dermatology and syphilology as a specialty and must limit his practice to dermatology and syphilology. The Board desires to appraise the applicant's educational opportunities, hospital and teaching positions, contributions to dermatologic literature, membership in medical societies and general reputation.

Each applicant will be required to fill out the detailed application blank to be obtained from the secretary and to comply with other requirements, including the payment of a fee.

The by-laws provide for the classification in three groups of those who apply for certificates as follows:

The founders' group consists of dermatologists and syphilologists whose professional training, attainments and prestige entitle them, in the opinion of the Board, to a certificate without examination. Membership in this group can be obtained only during the first two years following the organization of the Board.

Group A consists of physicians who have practiced dermatology and syphilology ten or more years. Such applicants, whose training, in the opinion of the Board, shall have been adequate, are required to pass an oral examination (which will be both clinical and pathologic).

Group B consists of physicians who have practiced dermatology and syphilology at least five years, including their period of training. Such applicants must have had at least two years of special training in dermatology and syphilology, including at least one year in a well organized clinic or as an assistant in the private practice of a well known specialist in this field.

Written examinations will be held simultaneously at stated intervals in different parts of the country and will be required only of members of Group B. Each examination paper will be read by an examiner living in a district remote from that of the candidate.

Oral examinations will be held near the time and place of the annual meeting of the American Medical Association. This will be given to all members of groups A and B. The Board will endeavor to adapt this examination to the candidate's experience and years of practice. It will try especially to ascertain the breadth of his clinical experience, his knowledge of recent literature of dermatology and syphilology and his general qualifications as a specialist in this branch of medicine.

A certificate will be issued to each candidate who meets the requirements of the Board to the effect that the holder of the certificate has had adequate training in dermatology and syphilology and has successfully fulfilled the requirements of the Board.

It is expected that medical schools, hospitals and physicians, as well as the lay public, will utilize the certificate from this Board as a proof of adequate preparation in the field of dermatology and syphilology and of fitness of candidates for positions under their control. For this purpose lists of those holding certificates from this Board will be available for inspection and will be published from time to time by the Board.

A certificate granted by this Board does not of itself confer any degree or legal qualifications or license to practice dermatology or syphilology. The Board does not intend to limit or interfere with the professional activity of any duly licensed physician. Its aim is to elevate the standard of qualifications for specialists in our field and to certify as specialists those who voluntarily comply with the requirements of the Board.

HOWARD FOX, M.D.

EXHIBIT ON DERMATOLOGY AND SYPHILOLOGY AT MILWAUKEE

The Section on Dermatology and Syphilology of the American Medical Association has appointed a special committee on section exhibit to cooperate with the Committee on Scientific Exhibit in promoting an exhibit on dermatology and syphilology for the Milwaukee Session of the American Medical Association, June 12 to 16, 1933. The special committee consists of Fred D. Weidman, chairman, Philadelphia; Clark W. Finnerud, Chicago; Robert L. Gilman, Philadelphia; Hamilton Montgomery, Rochester, Minn., and Lester M. Wieder, Milwaukee. The closing date for applications is February 13. Application blanks for the exhibit may be obtained from members of the committee, or from the Director, Scientific Exhibit, 535 North Dearborn Street, Chicago.

Editorial

FIFTIETH ANNIVERSARY OF ARCHIVES OF DERMATOLOGY

The ARCHIVES OF DERMATOLOGY has had an important anniversary. With the volume beginning with this number it enters the second half century of its existence. January is not exactly its birth month, for the first number was issued in October, 1882, but the first volume contained fifteen numbers, and ended with December, 1883. As it is convenient to consider January 1 its anniversary, like royalty the ARCHIVES is choosing its own date. It hopes that it may claim without immodesty that it has had a useful and somewhat distinguished career.

At the time of its establishment there were five journals in the same field, but none in English. It began under favorable auspices, and one has a thrill of pride when one looks over the first number and the first volume. Volume 1, number 1, bears the date October, 1882. The editors were Henry G. Piffard and Prince A. Morrow; the publishers, William Wood & Company, New York.

Even this first volume has a modern look. The title of the first article in the first volume has a familiar ring: Trichophytosis—"Trichophytosis Cruris"—by George Henry Fox. The subsequent numbers in volume 1 have as contributors the well known men of that generation of American dermatology. Bronson, Bulkley, Fox, Hardaway, Hyde, Morrow, Piffard, Robinson, Sherwood, Taylor are the most familiar names, and McCall-Anderson and Unna give the publication a European flavor.

From that time to the present the ARCHIVES has continued without interruption. The first name was the best that it has ever had: the *Journal of Cutaneous Diseases*. There were some additions to the name from time to time to include the venereal diseases, and then in 1920 it was unfortunately changed to the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY.

In 1886 Morrow became sole editor. In 1889 he was joined by Fordyce. In 1892 Fordyce became the editor alone, and in 1896 he was joined by Johnston. In 1897 Swinburne joined Johnston, and in 1898 Lapowski joined these two. They continued until 1904, when Mewborn became editor with an editorial board. With all these editors the position was not only a labor of love but also of considerable expense. Morrow and Fordyce, particularly, contributed largely to its support. In 1909 McKee became editor, with the same board, and the ARCHIVES

was edited by him until the end of 1919. During this period the deficit in publication was met by a group of members of the American Dermatological Association, which had become the owner. In 1919 this burden had become so heavy that the life of the journal was threatened. Then the American Medical Association came to its support. Beginning in January, 1917, the Association had begun its publication at actual cost for the American Dermatological Association The ARCHIVES became the property of the American Medical Association in 1919, and since 1920 has been one of its journals. Through the generous support of the American Medical Association it has been able to flourish and enlarge. After the volume for 1883, in which fifteen monthly numbers were published, including October, November and December, 1882, a volume was issued each year up to and including 1919. Beginning with 1920 two volumes have been issued annually. There are thirty-seven volumes of the *Journal of Cutaneous Diseases* and twenty-six of the ARCHIVES OF DERMATOLOGY. These sixty-three volumes represent the story of dermatology in the United States during the fifty years of its great activity.

From the start the journal has been an epitome of dermatology. In a scientific sense it always flourished. At the present time the chief difficulty is that dermatology is so flourishing that the ARCHIVES has an embarrassment of riches in the material that is offered it. Its hope is that it may long continue to reflect a state of dermatology as vigorous as that which now exists.

W. A. P.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

TREATMENT OF CARDIOVASCULAR SYPHILIS. H. H. HAZEN, Am. J. Syph. **16**:289 (July) 1932.

In a review of the literature on the treatment of cardiovascular syphilis, Hazen emphasizes certain points that have been brought out by various authors, all of whom have agreed that each patient must have proper general medication. Impending, or the actual presence of, congestive failure calls for rest in bed in Fowler's position and a diet low in bulk and minerals in which fluid and salt are kept at a minimum. Stimulation of the heart must be correctly employed and diuretics and sedatives used when necessary. It is generally agreed that in congestive failure, antisyphilitic medication should not be given until compensation is reestablished. All authors agree that any course of treatment should be begun with mercury, bismuth or possibly the iodides, to prevent a chance Herxheimer reaction. Wile alone believes in using tryparsamide, although practically all other authors recommend small doses of neoarsphenamine at a later date. It is likewise agreed that in cases of coronary disease arsphenamine should not be employed. In cases of chronic myocarditis the reports are divergent, but, on the whole, they favor the use of the metals rather than the arsenicals.

Regarding the effects of therapy, there is marked discrepancy, perhaps owing to the varying standards of antisyphilitic medication employed. Hazen states that there are scores of papers dealing with the treatment of cardiovascular syphilis, all equally valueless because of their failure to indicate the number of patients treated or the variety of the antisyphilitic or cardiac medication employed.

The author reports on patients with cardiovascular syphilis who were seen in the ward of Freeman's Hospital during the period from 1911 to 1917. Practically all were Negro laborers. All patients were hospitalized as long as necessary, and the general treatment was carefully supervised. The treatment given all patients consisted of one course of old arsphenamine and a long course of injections of mercuric salicylate. In the treated patients, there was not a single death or even a severe reaction, but there were many nitritoid crises. The patients were given antisyphilitic therapy, and the controls were given identically the same general therapy. Fifty patients with aneurysm of the aorta were observed. Ten of them served as controls, and the average duration of life from the beginning of symptoms was eleven months, while in the treated cases, the average duration was thirty months. Of the forty-eight cases of aortic insufficiency observed, the majority of patients entered the hospital with mild congestive failure. Treatment was not started until compensation was established. For twelve untreated patients, the life expectancy from onset of symptoms was thirty-six months; for thirty-six treated patients, only forty months. Fifteen patients with syphilitic aortitis were treated; eight were improved and seven were not helped. Two patients with heart block and two with early syphilitic myocarditis were treated, with excellent results. Five patients with myocarditis developing in late syphilis were treated. One died in about six months; the others showed no change for one year.

The report shows that arsphenamine is borne much better than is usually stated, and that treatment is of decided value in certain types of syphilitic cardiovascular disease.

SYPHILIS AND TRAUMA WITH SPECIAL REFERENCE TO THE TARNOWSKY TEST. S. S. GREENBAUM and B. MADDEN, Am. J. Syph. **16**:297 (July) 1932.

In 1877, Tarnowsky improvised a cutaneous test for the diagnosis of syphilis. It consisted in the application of a caustic paste to the skin of the patient suspected

of having syphilis, with the idea of producing syphilitic phenomena through irritation of the skin, based on the supposition that in patients with syphilis, syphilitic lesions are more apt to develop in the areas that have undergone irritation. The test was considered positive if characteristic syphilitic lesions developed at the site of the cauterization.

Tarnowsky's conclusions in part were: In early syphilis, the test is more liable to be positive, especially in the secondary stage. In visceral and osseous syphilis and in the gummatous period of syphilis the test is often negative.

The authors mention previous experimental work done on the relationship between syphilis and trauma, and discuss the difficulties in an attempt to establish this relationship clinically. Their object in the present study was to determine, by dark-field and biologic methods the presence or absence of Spirochaeta pallida in the fluid content of blebs produced artificially in patients with acute and chronic cases of syphilis. They were not so much interested in proving a relationship between syphilis and trauma as in attempting to explain such a relationship. Blebs were produced by means of solidified carbon dioxide. The authors emphasize that in patients with secondary syphilis only those areas of skin were traumatized that presented no visible lesions of syphilis. In none of the nineteen patients studied was Spirochaeta pallida found either on dark-field examination of the bleb fluid or following the intratesticular inoculation of a primary and secondary series of rabbits with the bleb fluid. Even gumma-like ulcers which developed in some of the patients failed to show Spirochaeta pallida. They conclude that it would seem that Spirochaeta pallida is not directly concerned in the production of a syphilitic response to trauma.

THE INCIDENCE OF SYPHILIS IN PRIVATE PRACTICE AMONG NEGROES. W. R. R. GRANGER, Am. J. Syph. **16**:303 (July) 1932.

Because of the discrepancy in the reports in the literature on the incidence of syphilis among Negroes, the author gives the results of Wassermann tests performed on specimens of blood from 2,000 consecutively examined colored patients.

In 2,000 tests, 218 reactions were 4 plus; 77, 3 plus; 27, 2 plus; 46, 1 plus, 91, doubtful, and 49, atypical. Other specimens were hemolyzed, and in 1,492 cases the results were negative; giving 14.75 per cent strongly positive (3 plus or over), 8 per cent doubtful and 70 per cent negative reactions.

ANIONIC BISMUTH THERAPY IN NEUROSYPHILIS. H. G. MEHRTENS and P. S. POUPPIRT, Am. J. Syph. **16**:373 (July) 1932.

The problem of bismuth penetration into the central nervous system has received scant attention in the literature. The authors have made many efforts to cause bismuth injected into the muscles to appear in the spinal fluid, only to fail in most cases. The bismuth compounds in general use which the authors have been unsuccessful in causing to enter the central nervous system had their bismuth in the form of the cation. On theoretical grounds, the authors reasoned that bismuth might pass from the blood to the central nervous system if the bismuth were in anionic form. Dr. P. J. Hanzlik chose from the anionic bismuth compounds sodium iodibismuthite, of which he was able to dissolve 6 per cent in ethyl glycol containing 12 per cent of sodium iodide. He named the product, which was definitely proved to be anionic, iodobismitol.

The penetration of this drug into the brain of animals and into the brain and spinal fluid of man was studied. Two moribund patients who received injections of iodobismitol showed bismuth in the brain. Of forty-two patients treated with the drug, 92 per cent showed bismuth in the spinal fluid. The drug was clinically as effective in experimental syphilis of rabbits and on the primary and secondary lesions of man as would be expected from a readily absorbable bismuth product. In a series of one hundred cases of neurosyphilis, the results after two years seemed better than any they had had from any cationic bismuth preparation. They

did not feel justified, however, in maintaining the whole group on one mode of therapy alone.

The authors are inclined to consider that in regard to bismuth, there is a correlation between its electronegative form, penetrability into the central nervous system and therapeutic efficiency. The hypotheses that naturally suggest themselves are: that the clinical usefulness of any bismuth preparation for neurosyphilitic conditions is dependent on its ability to assume an electronegative form; that possibly all bismuth compounds, under certain conditions, furnish anionic bismuth to a greater or less degree, thus explaining their varying therapeutic usefulness; that the greater the ability of the preparation to yield available electronegative bismuth, the greater may be its therapeutic success.

THE EFFECT OF INGESTION OF ALCOHOL ON THE WASSERMANN, KAHN AND HINTON TESTS. J. W. BRITTINGHAM and S. F. ROSEN, Am. J. Syph. **16**:403 (July) 1932.

Because of the prevailing belief that alcohol tends to change Wassermann reactions from positive to negative, the authors carried out the present study, with the following conclusions: The effect of the ingestion of alcohol on the Wassermann reaction has been overestimated. Alcohol had no appreciable effect on the Wassermann, Kahn and Hinton tests in eighteen patients with untreated syphilis. The discrepancy between the opinion based on these results and many prevailing opinions is probably due to the greater sensitivity of modern serologic technic.

REUTER, Milwaukee.

HEMOCHROMATOSIS AND PURPURA. R. P. STETSON and H. W. FERRIS, Arch. Int. Med. **50**:232 (Aug. 1) 1932.

Two cases of hemochromatosis are reported in which purpuric symptoms were so pronounced that a diagnosis of scurvy was suggested. A discussion is also given of the possible mechanism for the development of the hemorrhagic manifestations, and the suggestion is made that hemochromatosis may predispose to scurvy.

JAMIESON, Detroit.

CONTACT DERMATITIS IN AN ANESTHETIST, DUE TO "AVERTIN." G. V. KULCHAR, J. A. M. A. **99**:560 (Aug. 13) 1932.

Local sensitization to avertin (tribromethanol) developed in an anesthetist after he had handled this preparation for eleven months, and an erythematosquamous dermatitis developed on the hands. The eruption was aggravated by every exposure to the irritant but disappeared rapidly when protective measures were used. Patch tests with avertin resulted in a vesicular dermatitis. Attempts at passive transfer of the sensitiveness were unsuccessful.

SCLEREDEMA ADULTORUM (BUSCHKE). NORMAN N. EPSTEIN, J. A. M. A. **99**:820 (Sept. 3) 1932.

The author reports two cases of scleredema adultorum in each of which there were recurrence and an acute infection preceding both attacks. He feels that the disease may be a type of elephantiasis secondary to the preceding acute infection. It is differentiated from scleroderma clearly, and is shown to be similar to sclerema neonatorum. Forty-one cases previously reported abroad are reviewed.

INDUSTRIAL DERMATOSES. EARL D. OSBORNE and EDWIN D. PUTNAM, J. A. M. A. **99**:972 (Sept. 17) 1932.

The authors review 216 cases of industrial dermatoses due to allergy. A latent period was present between the first exposure and the development of the

dermatitis. In two workers with normal skins who were exposed to a sulphonated oil, patch tests were made daily up to the time the dermatitis developed. The patch test became positive simultaneously with the appearance of the dermatitis on the exposed parts. The authors discuss the relationship of mycotic dermatitis to industrial dermatoses and consider the question of compensation in both conditions.

LYMPHOGRANULOMA INGUINALE. H. F. DEWOLF and J. V. VAN CLEVE, J. A. M. A. **99**:1065 (Sept. 24) 1932.

This is the first report of a large series of cases of lymphogranuloma inguinale in this country. Antigens were prepared from eleven patients suffering from the disease, and the Frei test was applied to 1,010 patients. Fifty-eight patients gave definitely positive reactions; of these, thirty-one had active involvement of the inguinal glands, four had scars of healed inguinal adenitis, which had been active from two to four and a half years prior to the application of the test; twenty gave a history of having had persistent inguinal adenitis five to twenty-five years previously, and three suffered from the anorectal syndrome. The authors believe that lymphogranuloma inguinale is a specific venereal disease, and that the Frei test is a specific means of diagnosis.

CARO, Chicago.

THE OCCURRENCE OF BOILS AMONG MEN WORKING IN COAL MINES. S. W. FISHER, J. Indust. Hyg. **14**:243 (Sept.) 1932.

Twenty-nine mines were inspected and two hundred miners examined to determine the causation of occasional outbreaks of boils among British coal miners. These outbreaks did not present a serious problem, except in a few isolated instances. The main factor in the causation of boils in the men working underground, apart from individual predisposition to this form of infection, appeared to lie in the high wet bulb temperature (75 F. and higher) in which the men worked; the vitality of the organisms was increased through warmth and moisture, and the entry of the staphylococcus into the skin was facilitated by the dilatation of the orifices of the sweat glands and hair follicles.

CUTANEOUS PAPILLOMAS AMONG PATENT FUEL WORKERS IN RELATION TO MALIGNANT DISEASE. C. C. R. DOWNING, J. Indust. Hyg. **14**:255 (Sept.) 1932.

The author quotes the findings of the Departmental Committee on Compensation for Industrial Diseases in England in 1907 that "men engaged in handling pitch or other tarry products are liable to suffer from warty growths which ulcerate and occasionally become the seat of epitheliomatous cancer." These papillomas occur most commonly on the face, hands and scrotum, and in the age group of 40 to 60 constitute the greatest industrial hazard to which the patent fuel worker is subjected. Sessile papillomas are regarded as potential epitheliomas, whereas the pedunculated type never becomes cancerous, in the experience of the author. The length of time necessary for a sessile pitch papilloma to develop into an epithelioma varies from weeks to years. The lesions may appear with less than five years of exposure, but on the average, they appear after more than ten years, and they may develop in a person several years after exposure to the pitch. In the author's experience with seventy-nine cases of epithelioma and pitch papillomas none of the patients had died, the epitheliomas being of a relatively benign form. The author recommends the use of radium in the form of radon seeds for the larger growths and excision for the smaller, and he has obtained good results in treating the papillomas with carbon dioxide snow and diathermy.

WIEDER, Milwaukee.

STAPHYLOCOCCUS AUREUS: DISSOCIATION AND ITS RELATION TO INFECTION AND TO IMMUNITY. RACHEL E. HOFFSTADT and GUY P. YOUMANS, J. Infect. Dis. **51**:216 (Sept.-Oct.) 1932.

The purposes of the experiments were to dissociate Staphylococcus aureus, if possible, and to study the relation between the dissociated forms in their invasive power in the animal and in their production of immunity. As a result of this work, the authors concluded that Staph. aureus can be dissociated into three forms. There are cross-agglutination and cross-complement fixation for all these forms. In animals treated with heat-killed cultures of the "whole" or of the dissociate forms the power of invasion of either the "whole" or the dissociated forms is not affected. The dissociated forms are only part of a normal cycle of changes through which the organism passes. The persistence of the avirulent form in the body of the animal may explain how the organism lurks in the body without manifestation and later, when virulence returns, appears again with lesions.

TULAREMIA: ACCURATE AND EARLIER DIAGNOSIS BY MEANS OF THE INTRADERMAL REACTION. LEE FOSHAY, J. Infect. Dis. **51**:286, (Sept.-Oct.) 1932.

The usefulness of the intradermal test for diagnosing tularemia is confirmed. This test is the earliest available diagnostic aid, becoming positive as early as the fourth day of illness or about a week before agglutinins usually appear in the blood. Positive reactions occur only in tularemia and not in normal persons or in those with other diseases. The positive reactions may become negative by artificial desensitization. This change appears to coincide with, and to depend on the induction of, adequate immunity. Subsequent resensitization has not occurred during the seven months following such desensitization. This is further proof that chemical detoxification of bacterial bodies can be carried to a reasonably satisfactory degree without noticeably impairing their antigenic properties. Daily subcutaneous injections of detoxified vaccine seem to have shortened the course of the disease in three cases. In spite of this, however, the author does not feel that this is an ideal form of treatment.

BACTERICIDAL ACTION OF PHENYL-MERCURY-NITRATE; FURTHER OBSERVATIONS. L. A. WEED and E. E. ECKER, J. Infect. Dis. **51**:309 (Sept.-Oct.) 1932.

In a previous report attention was called to the high bactericidal and fungicidal action and low toxicity for animals of phenyl-mercury-nitrate. The present report is concerned with a phase of the problem created by existing criticisms concerning the testing of disinfectant action and offers additional data substantiating earlier claims. The previous findings are confirmed by the present report. The bactericidal action of phenyl-mercury-nitrate is not selective. The presence of renal tissue does not decrease the bactericidal action of the compound, while that of hepatic tissue does.

IMMUNOLOGIC STUDIES ON TULAREMIA IN RABBITS. CORNELIA M. DOWNS, J. Infect. Dis. **51**:315 (Sept.-Oct.) 1932.

In these experiments an attempt was made to correlate functional and structural changes of tissues in immunity. Rabbits were immunized with formaldehydized cultures of Pasteurella tularensis. This immunity was evidenced by a delay of invasion of the blood stream by the organism, the production of agglutinins in the blood stream and the marked proliferative and localizing changes shown in the lesions in immune animals as contrasted with normal controls. This immunity develops slowly after from six to eight injections. Subcutaneous, intracutaneous or intravenous injections are equally effective. The author suggests that a similar method of immunization might be effective in man. CORNBLEET, Chicago.

CHEILITIS GLANDULARIS. J. M. DE LOS REYES, United Fruit Company, Twentieth Medical Report, 1931, p. 193.

The author cured a patient whose lower lip was involved by means of electrodesiccation of the glands under local anesthesia. The discharge ceased; the inflammation subsided, and the lip decreased in size. RATTNER, Chicago.

YAWS AND SYPHILIS IN CALABAR, SOUTHERN NIGERIA: AN ANALYSIS OF 5,000 SACHS-GEORGI TESTS. SAINT C. RAMSAY, Ann. Trop. Med. **26**:149 (July 14) 1932.

Two thousand, six hundred children between the ages of 4 and 16 and 2,400 adults were examined serologically.

The charts show a gradual decrease in the number of positive tests from the age of 7 to 16, the average percentage of positive tests being 35.6 per cent. Above the age of 16, there was gradual increase up to the age of 42, at which period 50 per cent of the tests were positive. The view is given that the gradual lowering of the percentage of positive reactions in children indicates the tendency of yaws to spontaneous cure. For adults, however, a positive test might mean yaws, syphilis, or both, and therefore the gradual increase of positive tests cannot be ascribed to yaws or syphilis alone, but may be due to either or both or to reinfection with yaws. JAMIESON, Detroit.

A WARD OUTBREAK OF ERYTHEMA NODOSUM. NORMAN D. BEGG, Brit. J. Child. Dis. **29**:343 (July-Sept.) 1932.

An outbreak of four cases of erythema nodosum occurred in a ward containing twelve children convalescing from whooping cough. All the children were under 6 years of age. The four children with erythema nodosum all reacted strongly to the Mantoux test, and in each case there was roentgenologic evidence that suggested involvement of the hilar glands. Eight days before the first case occurred, there had been a child in the ward with acute miliary tuberculosis to whom all the children had been exposed. In new patients who had been exposed to the children with erythema nodosum but not to the child with miliary tuberculosis erythema nodosum did not develop, which is evidence that the latter is not a specific infective disease.

HERPES ZOSTER AND VARICELLA IN THE TROPICS. E. G. SAYERS, Brit. M. J. **2**:402 (Aug. 27) 1932.

Two examples of cases of herpes zoster giving rise to varicella are recorded. The varicella occurred in boys of 14 and 16 years respectively; the herpes, in adults. The patients were inhabitants of the British Solomon Islands, a rather isolated region with a small population scattered over many different small islands. In such a place the route of infection in any given epidemic is usually easy to trace. About twelve patients had chickenpox, and in tracing the source it was found that the first patient had been exposed to a case of herpes zoster. The second example was even more direct. A man became ill with herpes zoster, and sixteen days later his house boy who had attended him had varicella.

THE USES OF NON-SPECIFIC PROTEIN THERAPY. R. CRANSTON-LOW, Brit. M. J. **2**:597 (Sept. 24) 1932.

This paper summarizes the recent advances in nonspecific protein therapy, a treatment which the author considers to be based on rational and scientific foundations. There are several theories as to the mode of action. The author favors the view that the active agent is a product of protein decomposition. The washing of tissue fluids into the circulation produces changes in the blood, such as leukopenia followed by leukocytosis, increase in young and atypical erythrocytes and platelets, increase in fibrinogen, globulin, thrombokinase and blood sugar in the nonprotein nitrogen content and in the proteolytic ferments and finally an

increase in the permeability of the cell membranes and capillaries. Some workers believe that in addition to the stimulation of the body cells to antibacterial activity there is a stimulation of the internal secreting glands and the bone marrow. It is also thought that specific antibodies are liberated by the injections, or that sessile antibodies are thrown into the circulation. Recently it has been shown that the leukocytosis which follows leukopenia is no more than the normal fluctuation, such as is seen after the taking of food; so the leukocytosis is not responsible for the results obtained, nor is a rise in temperature essential for a successful result. Which of the many changes occurring after injections of protein are essential is still in doubt. The various diseases of the skin in which nonspecific therapy has been used are then considered separately. Included are urticaria, eczema, neurodermatitis, exfoliative dermatitis, pemphigus, lupus erythematosus and syphilis. The author concludes that this form of therapy is of decided benefit in conditions due to sensitization or in which sensitization is suspected. It should not replace specific therapy, it should not be used as a routine, and the best results are obtained when it is used in combination with other measures. It is not important which form of protein is used — hemotherapy, milk, turpentine, bacterial vaccines and other forms of medication give equally good results. The chief contraindications are alcoholism and myocardial disease.

A Case of Ichthyosis Hystrix. T. B. Sellors, Brit. M. J. **2**:630 (Oct. 1) 1932.

This case is reported only because it is probably the most extensive one on record. Lesions were distributed over the whole trunk, neck, axillae and groins. The patient was 16 years of age, and until three years previously the lesions were so pale that they attracted no attention. In the past three years they had become dark brown and in places were actually black. A photograph accompanies the article.

Treatment of Inflammatory Conditions by Radiation. J. H. Douglas Webster, Brit. M. J. **2**:665 (Oct. 8) 1932.

Among the inflammatory conditions which respond well to irradiation with roentgen rays are furuncle, carbuncle, whitlow and erysipelas. The dosage recommended is from 15 to 20 per cent surface doses. The roentgen rays cause destruction of organisms and changes similar to those in inflammation, engorgement of vessels and lymph glands, and diapedesis in the part irradiated. There are produced also protein shock due to damage to the blood and tissue cells, chemical action on cell ferments and probably reactive regeneration stimulation, as is shown by the proliferation of fibroblasts. The remainder of the paper deals with the treatment with roentgen rays of specific infections and entities, such as actinomycosis, tuberculosis, sinusitis and arthritis.

Rattner, Chicago.

Diseases of the Australian Aborigines. H. Basedow, J. Trop. Med. **35**:193 (July 1); 209 (July 15); 247 (Aug. 15) 1932.

Dermatoses reported among the aborigines included erysipelas, which occurred rarely, a case of actinomycosis, syphilis, which has been found only since the advent of the white race, leprosy, yaws, gangosa, ulcerative granuloma of the pudenda, pediculosis, scurvy, eczema, acne vulgaris, acne tropica, impetigo and scabies.

Jamieson, Detroit.

A Case of Symmetrical Hyperkeratosis of the Lower Extremities. J. A. Pires de Lima, Ann. de dermat. et syph. **3**:345 (April) 1932.

A curious form of hyperkeratosis of the feet in a man, aged 22, is recorded. The condition of the soles presented the usual picture of symmetrical keratoderma, plus onychogryphosis of the toe-nails (a rare accompaniment), but the heels exhibited an arresting phenomenon. From them projected a mass of keratotic

tissue in the form of a truncated cone, 18 cm. in height and 30 cm. at its maximum circumference. The condition was hereditary, the father and the grandfather being similarly afflicted. The Wassermann reaction of the patient's spinal fluid was slightly positive. Following surgical intervention and local roentgen therapy, he was given antisyphilitic treatment. The article is well illustrated, including roentgenograms.

A Case of Parapsoriasis Varioliforme. M. Goldenberg and D. Bychowsky, Ann. de dermat. et syph. **3**:349 (April) 1932.

A case of pityriasis lichenoides et varioliformis acuta in a woman of 35 is reported, though the author prefers the designation of parapsoriasis varioliforme. The eruption was rather classic in morphologic characteristics and clinical evolution, the interesting feature being the undoubted presence of tuberculosis, which raises again the question of the etiologic rôle of tuberculosis in this peculiar disorder.

Bromoderma of the New-Born; Experimental Cutaneous Reactions. Sezary, Lefèvre and Horowitz, Bull. Soc. franç. de dermat. et syph. **39**:508 (April) 1932.

In a 7 months old infant who had been given a bromide mixture a bullous dermatitis developed. Skin tests were performed as follows: A scratch test was made on one arm, a 100 per cent solution of sodium bromide being used and a physiologic solution of sodium chloride as a control, and intradermal injections of each solution were made on the other arm. At the site of injection a red papule developed quickly, but vanished entirely within twenty-four hours. On the other hand, a papule did not appear at the site of scarification until three days later, and it was followed on the seventh day by a bulla conforming in every respect to the bullae of the eruption. The "cuti-reaction" was thus more reliable than the "intradermo-reaction," and proved beyond doubt the culpability of the bromide.

Macular Cutaneous Atrophy of Tuberculous Origin. Gougerot, J. Meyer and Weill-Spire, Bull. Soc. franç. de dermat. et syph. **39**:523 (April) 1932.

A woman, aged 32, presented two dermatologic conditions: atrophic plaques on the arms of eighteen months' duration and subcutaneous nodules on the legs of twelve months' duration. Among the atrophic lesions the principal plaque contained in its center a small nodule highly suggestive of a tubercle. In the case of the lesions of the legs a clinical differentiation between gumma, sarcoid, and erythema induratum was well nigh impossible. Although further clinical signs were lacking and serologic tests had been repeatedly negative, the patient had suffered two miscarriages, and the family history was suggestive of a syphilitic background. No decision had been reached as to whether the condition was syphilis or tuberculosis. Thus the title of the article is misleading.

Epithelioma, Lupus and Pityriasis Rosea in a Child of Ten Years. M. B. Saad, Bull. Soc. franç. de dermat. et syph. **39**:552 (April) 1932.

This case is placed on record because of the extreme youth of the patient (10 years) in whom a prickle cell epithelioma developed in lupus tissue, the diagnosis being incontestably established by microscopic examination. A classic case of pityriasis rosea was likewise present.

Gandy, Houston, Texas.

Bismuth Erythroderma. J. Nicolas and J. Rousset, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Lyon) **39**:474 (April) 1932.

The authors report a case of generalized exfoliative dermatitis due to bismuth, comparable in every particular to a postarsphenamine dermatitis.

FOX-FORDYCE DISEASE. G. DEL VIVO, Gior. ital. di dermat. e sif. **73**:1257 (Aug.) 1932.

The author reports a case of Fox-Fordyce disease in a woman, aged 39, who was under observation for about three years, during which time she received opotherapeutic treatment, roentgen irradiation, actinotherapy and various other treatments without improvement. Sections of the skin of the axillae showed degenerative changes of the epithelium of the apocrine glands. Around the affected tubuli there was an infiltration of lymphocytes and fibroblasts. The author concludes that Fox-Fordyce disease is essentially a sudoriparous apocrinitis.

RESEARCHES ON CUTIS MARMORATA. M. COMEL, Gior. ital. di dermat. e sif. **73**:1282 (Aug.) 1932.

Several cases of cutis marmorata were studied in order to determine the mechanism of the cutaneous vascular disturbance. General and local temperatures were recorded under different conditions, and dermographic reactivity, response to thermic stimuli and response to epinephrine and histamine were studied. From these observations the author concludes that the cutaneous vascular disturbance of livedo (cutis marmorata) is due to certain phenomena taking place in the capillaries and not in the arterioli of the skin. Vascular stimulation under certain conditions may cause the disappearance of the vascular network of the skin or its transformation from annular cyanosis (cutis marmorata) to erythema annulare. The phenomena observed in livedo or cutis marmorata may be explained hypothetically as due to an abnormal incapacity of the mechanism of vasoconstriction of the capillaries.

TRICHOSEBACEOUS CYSTIC NEVUS (STEATOCYSTOMA MULTIPLEX, PRINGLE). FRANCESCO LISI, Gior. ital. di dermat. e sif. **73**:1324 (Aug.) 1932.

A woman, aged 28, since puberty had had innumerable small cystic formations, slightly elevated, yellowish and containing sebaceous material. Histologically, these tumors were cysts lined with stratified epithelium and were connected with the ducts of the sebaceous glands. Some of the cysts had a papillomatous wall. The author considers the condition as nevic. He gives an excellent review of the literature.

CONTRIBUTION TO THE STUDY OF HERPES GESTATIONIS. ELIO SECHI, Gior. ital. di dermat. e sif. **73**:1353 (Aug.) 1932.

The author reports a case of herpes gestationis in a patient, aged 34, during her sixth pregnancy. The first symptoms of the disease had appeared several years before during her fourth pregnancy, the condition clearing up spontaneously after a normal delivery. During the fifth month of her sixth pregnancy she had a new outbreak, which was quickly controlled by the administration of extract of corpus luteum. Another outbreak shortly after delivery was similarly controlled. The author concludes that herpes gestationis is due to a disturbance of production of the corpus luteum hormone.

BIOLOGIC PROPERTIES OF THE SKIN. POSSIBILITY OF TRANSMITTING THESE PROPERTIES FROM ANIMAL TO ANIMAL BY MEANS OF CUTANEOUS TRANSPLANTATIONS. F. BERNUCCI, Gior. ital. di dermat. e sif. **73**:1373 (Aug.) 1932.

The skin being the seat of the production of defensive processes, several investigators have tried to prove their existence by transplanting pieces of skin to other animals. Trawinski, for example, after making rabbits immune to certain bacteria, removed large pieces of skin from these animals and transplanted them in toto to other nonimmune rabbits, with the result that after several days the blood serum of the latter animals showed specific agglutinins against the same

bacteria. This property was soon lost, usually after a month. The author has repeated these experiments and has found that the second or control animal presents in its serum not only agglutinins but hemolysins.

ULCUS VULVAE ACUTUM (LIPSCHÜTZ). G. NARDI, Gior. ital. di dermat. e sif. **73**:1414 (Aug.) 1932.

The author reports a case of the condition described by Lipschütz in 1912. The patient also had a syphilitic chancre, gonorrhea and venereal warts. There were three lesions of ulcus vulvae acutum, which were situated in both labia minora. Bacillus crassus was present in these ulcerations. Although this organism has not been proved to be the etiologic agent of this disease, its presence in large numbers in these lesions is of diagnostic value.

LIPOSOLUBLE SALTS OF BISMUTH. A. VIEIRA PIMENTEL, J. syph. **3**:138 (June) 1932.

The use of bismuth camphocarbonate dissolved in oil is highly recommended by the author, as it is the most active preparation of bismuth. He claims that from ten to twelve injections are sufficient to revert the Wassermann reaction, and that the chancre and other clinical manifestations disappear quickly under treatment with this substance. From the clinical point of view, the author considers this bismuth salt to be as effective as the arsphenamines. The only accident observed has been slight gingivitis.

HOOK NEEDLE FOOT A SIGN OF CONGENITAL SYPHILIS. M. TORROELLA, Gac. méd. de México **63**:353 (July) 1932.

The author describes a deformity of the feet in the new-born which consists in extreme flexion of the foot over the leg, giving the extremity the appearance of a knitting hooked needle. This condition seems to be due to a preponderance of the action of the flexor muscles of the leg. In some cases, the hypotonia is so extreme that the dorsum of the foot may be brought in contact with the anterior surface of the leg.

PARDO-CASTELLO, Havana, Cuba.

THE FINAL DESTINY OF SYPHILITIC PATIENTS TREATED WITH MALARIA. K. VON BERDE, Dermat. Wchnschr. **95**:1284 (Sept. 3) 1932.

Thirty patients with various types of syphilis were treated in 1925 by inoculation with malaria before any other treatment was instituted. From ten to twelve chills were allowed to occur, and then the malaria was cured with quinine. This was followed by a course of neoarsphenamine, a total of from 3 to 5 Gm. being given. No further treatment was given unless recurrence developed. Sixteen of the thirty patients were followed for from five to six years. Seven of them were apparently permanently cured serologically as well as clinically. These were treated mostly when the condition was in the early florid stage. No damage could be ascribed to this form of therapy.

ANIMAL CHARCOAL IN ECZEMA SOLARE. J. CSILLAG, Dermat. Wchnschr. **95**: 1328 (Sept. 10) 1932.

The author describes a patient who had had dermatitis on exposure to sunlight for fifteen years. Animal charcoal tablets desensitized her in a short time.

THE DIAGNOSIS OF LYMPHOGRANULOMATOSIS. ERWIN FUCHS, Dermat. Wchnschr. **95**:1329 (Sept. 10) 1932.

A brief review of the characteristics of Hodgkin's disease as well as some comments on the literature is followed by a case history of a man 42 years old. A

tumor of the nose developed, which was diagnosed as syphilis, later as tuberculosis and then as carcinoma. The final course of the condition was that of Hodgkin's disease, which was verified at autopsy.

THE INFLUENCE OF ATOPHAN, CALCIUM AND VIGANTOL ON THE IRRITABILITY OF THE SKIN. WALTER STEFFEN, Dermat. Wchnschr. **95**:1399 (Sept. 24) 1932.

The author used 106 persons without any cutaneous disorder as test subjects. He determined the dose of ultraviolet radiation which caused erythema, and for several days gave the subject the medication to be tested. He then repeated the determinations. He drew the following conclusions:

1. Atophan adminstered by mouth decreased the irritability in about one half of the cases.

2. Calcium gluconate administered by mouth also decreased the irritability in about one-half.

3. Calcium gluconate administered intravenously decreased the reactivity in more than half.

4. Vigantol produced no characteristic change.

5. The therapeutic use of atophan or calcium in combination with local therapy is apparently indicated in inflammatory conditions.

BAKERS' ECZEMA AND SENSITIVENESS TO LACTIC ACID. DESIDER KENEDY, Dermat. Wchnschr. **95**:1402 (Sept. 24) 1932.

In a case of bakers' dermatitis apparently due to rye flour dough, a sensitiveness to lactic acid was demonstrated by patch tests.

TEST OF SUSCEPTIBILITY TO ECZEMA IN PATIENTS WITHOUT CUTANEOUS ERUPTIONS, IN THOSE WITH ERUPTIONS AND IN ALLERGIC PERSONS: ITS PRACTICAL MEANING. ERNA ZITZKE, Dermat. Wchnschr. **95**:1425 (Oct. 1) 1932.

The author prepared saline extracts of seborrheic, psoriatic and normal human scales. These extracts were injected intracutaneously in dilutions of 1:10,000, 1:1,000 and 1:100. The test subjects included 65 noneczematous patients, of whom 26 had psoriasis or parasitic eruptions and 39 had normal skins, and 278 eczematous persons. In 13.8 per cent of the noneczematous and in 47.5 per cent of the eczematous patients the tests were positive with one or more of the extracts. This indicates that 13.8 per cent of apparently normal persons are susceptible to eczema if exposed to relatively slight irritation and should avoid industries exposing them to irritating substances.

TREATMENT OF HIDRADENITIS WITH ULTRAVIOLET RAYS. J. MENTCHIKOW, Dermat. Wchnschr. **95**:1435 (Oct. 1) 1932.

The author treated thirty-six patients with hidradenitis of the axilla with daily, constantly increasing doses of ultraviolet rays from a water-cooled quartz mercury vapor arc lamp. In more than half the condition entirely cleared up within ten days.

TUBERCULOSIS OF THE EXTERNAL GENITALIA FROM CONTACT INFECTION. H. VIETHEN, Dermat. Wchnschr. **95**:1469 (Oct. 8) 1932.

Two cases are described in which tuberculous ulceration occurred apparently as a result of external infection. In a boy, 10 years of age, tuberculosis of the prepuce developed secondary to a draining tuberculous inguinal gland. A girl, 15 years of age, presented a tuberculous ulceration extending from the labia onto the buttock. She had tuberculosis of the urinary tract.

TAUSSIG, San Francisco.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

LEO SPIEGEL, M.D., *Secretary*

May 3, 1932

JOSEPH J. ELLER, M.D., *Chairman, Presiding*

TERTIARY SYPHILODERM. Presented by DR. GEORGE C. ANDREWS.

Z. H., a colored woman, aged 34, had been presented in March, 1932, showing large, reddish, infiltrated plaques on the forehead, back of the neck, chest, back, arms and legs. When presented the second time the lesions were markedly improved. The patient had been given three injections of neoarsphenamine; after the last injection there was a reaction. The medication was changed to silver arsphenamine, and the patient received two injections. She received twelve injections of mercury. It was later learned that she had received antisyphilitic treatment five years previous to presentation. A daughter, aged 20, presented congenital syphilis (interstitial keratitis). The patient had a 4 plus Wassermann reaction of the spinal fluid and blood, and the reactions to old tuberculin and acid-fast inoculations were negative.

DISCUSSION

DR. SIGMUND POLLITZER: A positive Wassermann reaction is fairly common in leprosy, but this case does not suggest leprosy to me. The patient presents a type of syphiloderm that is common among the colored people in this country: circinate lesions with a delicate, slightly raised border. May I ask whether this woman has lived in a country where lepra occurs?

DR. A. BENSON CANNON: No, this woman has had no connection with a leper state, except for a short stay in Havana. She is a native of New York and Savannah, Ga.

DR. SIGMUND POLLITZER: That complicates the situation somewhat, because there is a fair amount of leprosy in Savannah, but I should not on that account change my diagnosis of syphilis.

DR. A. BENSON CANNON: We have studied the patient for a number of weeks, bearing in mind the possibility of her having leprosy, syphilis or tuberculosis of the sarcoid type. While the lesions were suggestive of leprosy, the absence of sensory disturbances in the lesion and our inability to find any other evidences of leprosy suggested more the possibility of sarcoid or syphilis. I have never observed similar lesions in leprosy without anesthesia. I have found that, even though macular lesions in leprosy may be so slight as almost to escape the attention of the trained eye, one always is able to find evidence of anesthesia as well as to demonstrate the pathologic process of leprosy and the lepra bacillus. We are well aware of the difficulty experienced in differentiating tuberculosis, leprosy and syphilis, both clinically and pathologically. I think that even though the patient has a strongly positive Wassermann reaction of the blood and spinal fluid, one can almost discount the possibility of the cutaneous condition being syphilitic because of the lack of improvement that she has shown following the amount of syphilitic treatment she has had. I think that she has a sarcoid type

of tuberculosis because of the absence of anesthesia, and because she does not respond to syphilitic treatment. Tuberculin reactions are not infrequently seen in the sarcoid type of tuberculosis.

DR. EUGENE TRAUB: At a recent meeting, Dr. Howard Fox presented a patient who had the tuberculoid type of leprosy. This patient had a large, single, annular lesion on the face very similar in character to the lesions shown by the present patient. The slightly raised elevated border, I distinctly recall, was a special feature of the case, presented by Dr. Fox, who drew attention to the fact that he had recently seen four or five similar cases, all of which showed a structure closely resembling tuberculosis microscopically; for this reason, the rather unsuitable name tuberculoid was applied to this special variety of leprosy.

TINEA SYCOSIS OF THE EYEBROW. Presented by DR. HERMAN SHARLIT.

L. C., aged 29, born in the United States, had complained of an eruption of two years' duration. The patient presented an erythematous, crusted, pustular, follicular eruption limited to the inner side of the left eyebrow. Under local treatment with ultraviolet rays, the eruption had cleared up, but recurred as soon as treatment was discontinued. Fungi were found in the sodium hydroxide preparations. The eyelids showed slight edema and crusting.

DISCUSSION

DR. CHARLES WOLF: The interesting feature is the finding of fungi; the unusual feature is that the condition has remained so localized over such a long period. In view of the fact that it has been present so long, one would expect a dermatophytid to have developed on the body.

DR. SIGMUND POLLITZER: What type of organism was found?

DR. HERMAN SHARLIT: The report did not specify the exact type; it merely stated that fungi were found.

DR. GEORGE M. LEWIS: Was the organism found in the hair or in the scales?

DR. HERMAN SHARLIT: I did not make the examination. I requested that a hair be plucked, and that a study of the hair be made. I assumed that this was done, and that the report was made on this basis.

DR. JOSEPH J. ELLER: What other treatment did the patient receive?

DR. HERMAN SHARLIT: Salves were used. We have not treated the patient very long.

DR. GEORGE M. LEWIS: If this is ringworm, it is a most unusual case. I have examined a number of similar lesions, but always with negative results. In scales it is necessary to find mycelium, since fat droplets may simulate spores and lead to an erroneous conclusion. There are healthy hairs present in the lesion, which do not pull out readily. I shall be interested to hear of the cultural findings.

DR. OSCAR LEVIN: The patient shows a circumscribed, inflammatory area of the eyebrow. There are edema, baldness due to falling out of the hair and evidence of inflammatory reaction. I consider this a case of tinea infection of the hair follicles of the eyebrow.

A CASE FOR DIAGNOSIS (LEUKEMIA?). Presented by DR. HERMAN GOODMAN.

The patient, aged 61, was first seen on April 21, 1932, at which time he presented a generalized erythema and thickening of the skin, with several palm-sized areas, most marked on the shoulders and the back. There were flat, dry erythematous macules of slightly brownish hue; some were crescent-shaped, and some oval-shaped. Two years prior to presentation the patient had had a severe generalized itching. He stated that his skin was reddened at that time. He

applied at a dispensary for treatment, but obtained no relief. The itching became more intense after that, and nothing seemed to give relief.

A biopsy was performed on April 21, 1932, and showed a thin, atrophic epidermis and a dense round cell infiltration ending abruptly at the lower margin of the middle corium. There was a dense round cell infiltration about the blood vessels. The exudate consisted of an increased number of blood vessels and a large number of lymphocytes.

The blood count showed 82 per cent hemoglobin, 4,400,000 red cells, 12,000 white cells, 33 per cent polymorphonuclears, 63 per cent lymphocytes and 4 per cent eosinophils.

DISCUSSION

DR. CHARLES WOLF: Examination of the patient revealed a generalized lymphadenopathy, and the lesions themselves are infiltrated plaques. There is a lymphocystosis of 62 per cent. I think that a diagnosis of lymphocytic leukemia should be considered.

DR. HERMAN GOODMAN: I thought of mycosis fungoides at first rather than leukemia, but the blood picture and the histologic picture would lead me to believe that leukemia is the better diagnosis.

ERYTHEMA INDURATUM WITH BULLOUS LESIONS. Presented by DR. SAMUEL PECK.

A woman, aged 34, had had a chronic disease of the legs characterized by continuous formation of subcutaneous nodules, which came to the surface, ulcerated and left scars. On the legs the patient showed a number of well defined scars at the site of the old lesions. In addition a number of purplish-red, sharply defined nodules were present, some of which were ulcerated; several showed on their surfaces a number of very large bullae which were filled with purulent material. A number of the bullae had ruptured and left shallow ulcerations with oozing surfaces.

The general physical examination showed no evidence of tuberculosis. The patient said that she had not taken any drugs. The laboratory examinations showed a negative Wassermann reaction. Intradermal injections of tuberculin (1:1,000) on two occasions were negative and on one slightly positive.

The characteristic changes were found in the cutis and showed many sharply defined infiltrations of cells, which were also found in the subcutis and in the subcutaneous fat. Many of these infiltrations were around the blood vessels, and were made up of many epithelioid cells, lymphocytes and plasma cells; in some a number of typical Langerhan's giant cells were also seen. There seemed to be beginning necrosis in the center of some of the nodules.

DISCUSSION

DR. CHARLES WOLF: In questioning the patient, an interesting point was brought out; i. e., she is in the habit of taking acetylsalicylic acid. I think a dose of this drug should be given to see if the bullae appear.

DR. A. BENSON CANNON: Many people who have had reactions to tuberculin respond with redness and bullous lesions at the site of the tuberculous lesions. I wondered if these bullae, so rare in Bazin's disease, could not be caused by the tuberculin rather than by the disease itself.

DR. HERMAN GOODMAN: Could a person get a focal reaction as violent as this attack at the site of the lesions, with a negative or doubtful reaction at the site of the injection?

DR. A. BENSON CANNON: I think so. We do get redness of tuberculous lesions without a local reaction in cases in which the tuberculin is given subcutaneously. That is also true in the use of organic luetin for gummatous lesions, in which instance one sometimes sees many bullae with redness at the site of the gumma without obtaining any local reaction.

DR. MARION SULZBERGER: I think Dr. Goodman's point should be considered. I have never seen Bazin's disease with bullous lesions. Regarding the reaction to tuberculin, if the injection is given subcutaneously, the local reaction at the site of the injection is sometimes not obtained, but a flare-up at the site of the lesions occurs. In hypersensitive patients the intradermal injection usually produces a local reaction at the site of injection. One would expect this reaction in the present case if the bullous reaction at the site of the lesions were due to tuberculin. This is, however, not necessarily always the case. That is one of the grave faults of the tuberculin test. Except in the Moro test, a different area of skin from the one in which the lesion appears is always tested, so that we do not get a picture of sensitivity to tuberculin at the site of the actual lesion but elsewhere. This sensitivity of another cutaneous area may correspond to the sensitivity at the site of the lesion but may also differ from it. There may also be an error due to time. The ideal (but of course impossible) test would be one performed prior to the appearance of the lesion and at its actual site. Regarding Bazin's disease, it must be remembered that tuberculids are clinical and morphologic pictures showing a type of immunologic reaction that may also be produced by many other infectious or noninfectious conditions (e. g., syphilis, leprosy, streptococcus infections, drug eruptions and similar conditions). It is difficult to establish a clinical diagnosis in an isolated case. The fact that the bullous lesions appeared in this case reminds one that many cases of erythema multiforme are being ascribed to tuberculosis.

DR. SAMUEL PECK: The patient has had the lesions on the legs for many years, but the single attack of a bullous reaction is of recent occurrence. Does the presenter offer this latter supervention as an essential part of the disease? This is very unlikely. I think that a more ready explanation of the bullous outbreak should be found in the reaction to some of the therapeutic or diagnostic measures indicated in the history.

NEVUS RETICULARIS ET PIGMENTOSUS. Presented by DR. OSCAR LEVIN.

W. D., a colored girl, aged 3, born in the United States, showed a generalized marble-like network occurring in large areas and most marked on the chest, back and extremities. The face was also involved. The network was made up of interlacing black lines and streaks, with formation of black, irregular lesions on the chest. The lungs showed pleurisy with effusion, an encapsulated pleural effusion at the base of the right lung and a lesser one over the right upper lobe. Some swelling of the hilar lymph nodes in the right paratracheal and tracheobronchial regions was present. The Mantoux and Pirquet tests were positive. The Wassermann test was negative, as was the urinalysis.

At biopsy, in the papillary bodies and papillary layers of the corium dilated spaces surrounded with fibrous and muscular tissue were discovered; the cells were very scant and irregularly shaped, arranged in nests and resembled endothelial cells. A diagnosis of plexiform lymphangiectasia was made.

DISCUSSION

DR. MARION SULZBERGER: I think there is no doubt from the appearance of the lesions and from the history of their existence from birth or shortly thereafter that pigmentary nevoid anomaly is present. The clinical picture is unusual. The bizarre shape of the pigment deposits, with larger central lesions of irregular or jagged outline, some roughly diamond-shaped or triangular, some irregular parallelograms, sending out spider-like radiating filaments, which often interlace, forms a characteristic picture. I believe that this clinical aspect is so striking that once seen it can scarcely be forgotten or confused with any other anomaly of pigment. These characteristic shapes, together with the distribution and color of the dermatosis, as well as the history, make it seem a probability approaching on certainty that the case is one of incontinentia pigmenti. Prof. Bruno Bloch

had me describe the first case of this kind that is recorded in the literature (*Arch. f. Dermat. u. Syph.* **154**:19, 1928). Similar cases were subsequently described by Naegeli, Siemens, Almkvist and others.

I believe that if Dr. Levin will take the trouble to work up this case, it will be well worth while. It is the first recorded in this country and, to my knowledge, the first ever seen in a Negro. Careful histologic examination should show an approximately normal epidermis, with perhaps slight irregularities or vacuolization in the basal cell layer. The characteristic feature is the great increase of chromatophores in the papillae and upper parts of the cutis, without marked increase of pigment in the melanoblasts of the epidermis. It would seem that in these cases the newly formed pigment is not restrained in the epidermis and passed upward as in the normal process. There appears to be pigment incontinence, which allows the pigment to drip into the cutis. This led to the choice of the name.

DR. OSCAR LEVIN: The condition of the skin has always impressed me as being unusual and interesting. The histologic findings are essentially those of lymphangiectasis, with increased pigmentation of the skin. The patient, however, is colored.

DERMATOPHYTOSIS AND DERMATOPHYTID. Presented by DR. OSCAR LEVIN.

J. D., a woman, aged 37, for eleven years prior to presentation had complained of an eruption of the hands, feet and vulva. She had been treated with local applications and had received two fractional roentgen exposures to her hands. Scrapings from the hands one year prior to presentation were positive for fungi, but the trichophytin test was negative.

The patient presented erythematous, scaly, crusted and fissured lesions of the hands and feet and to a less extent of the vulva region. Three weeks prior to presentation erythematous, slightly infiltrated lesions of the trunk and extremities had appeared, varying in size from that of a dime to that of a dollar, the center showing a slight scale. She had been treated in the gynecologic department for a pelvic condition for which she also received roentgen therapy. Fungi were demonstrated in scrapings from the hands, but could not be found in the scrapings from the lesions on the trunk.

DISCUSSION

DR. EUGENE TRAUB: This is one of the most unusual cases presented this evening, for several reasons: one, the fact that mycelium on the palms was found one and a half years before presentation and again in a recent examination. In our experience, the finding of mycelium on palmar lesions has been exceedingly rare. This case does not seem to be an especially suitable one in which to find the organism. It is therefore all the more unusual that it has again recently been found. The lesions on the palms have been present more or less continuously for eleven years. The eruption on the body has been present only two weeks. This brings up the second unusual feature, that is, that the eruption on the body, which is that of classic erythema multiforme with lesions on the iris, should be interpreted as a dermatophytid rather than as a mere coincidental eruption in a patient who has had a previous cutaneous condition of long standing.

DR. OSCAR LEVIN: We regard the generalized eruption as being trichophytid. Such lesions may occur secondary to primary lesions, subsequent to general reactions, as from injection of trichophytin or from local irritation, as by trauma of the primary focus. Various types of trichophytids have been reported. The lesions observed on the patient presented this evening were larger and showed more intense inflammatory reaction than is usually observed.

DR. S. H. SILVERS: This patient has had lesions of the hands and feet and vulva recurring at various times over a period of eleven years. About a year ago I studied the lesions of the hand for fungi. The results of both the slide examination and the cultures were positive, and the organism was identified as

Epidermophyton interdigitale. On return to the hospital, owing to the patient's most recent attack, examination of the lesions of the hands and the body was made by the laboratory staff, which reported positive findings for the lesions of the hand, but negative finding for the lesions on the body.

DR. VAN ALSTYNE CORNELL: The patient gives a history of taking many laxatives, which may be the cause of the erythema multiforme-like lesions on the arms.

DR. EUGENE TRAUB: The point I wish to emphasize is: Would an erythema multiforme-like eruption of iritic lesions, as presented in this patient, be a likely type of dermatophyid in any event, the focus of tinea being the palms, the feet apparently being free?

DR. S. H. SILVERS: A year ago cultures were made of the lesions of the hand. No cultures were made recently.

DR. HERMANN GOLDENBERG: Erythema multiforme as a trichophytid is rare but has been observed and described. I saw an extensive and characteristic case a few days ago in a patient of Dr. Samuel Peck with trichophytosis and erythema multiforme of the arms. The eruption had been present for ten days and disappeared a few days after I saw the patient.

DR. DAVID BLOOM: I should like to know the result of the trichophytin test. Of course, a positive reaction would not prove that the eruption is a dermatophytid, but if the trichophytin test is negative, there is certainly no justification for calling this erythema multiforme-like eruption dermatophytid.

DR. S. H. SILVERS: The lesions of erythema multiforme, which are limited to the trunk and upper part of the extremities, have been present for about three weeks, while the lesions on the hands, feet and vulva have been present on and off for a period of eleven years.

DR. A. BENSON CANNON: I have had occasion to observe two cases similar to this one, although with much more extensive lesions on the body, varying from 12 to 18 inches (30.48 to 45.72 cm.) in diameter, with very fine scales at the inner margins of the circular rings. In scales microscopically examined and cultured were found mycelium and spores of the same type that we demonstrated in scrapings taken from the lesions on the hands and feet.

I agree concerning the danger of using the diagnosis of dermatophytid. There should be some substantiating evidence for such a diagnosis. One cannot do much more than examine each case from all points of view. The fact that many cases are "ids," however, must be recognized, and the conception of dermatophytid of the hands is backed by more evidence than most medical conceptions. It has back of it clinical observation and experiment, as well as immunologic, histologic and mycologic evidence and far-reaching analogies in animal experimentation. Furthermore, it is in most respects parallel to modern observations in many other infectious and noninfectious processes with evidences of transitory and practically asymptomatic bacillemias and toxemias, and occasional selective areas of hypersensitiveness.

DR. CHARLES WOLF: I do not see why a patient who has had trichophytosis on many parts of the body is not susceptible to toxic eruptions from other causes. Erythema multiforme is just a manifestation of a toxic infectious process. It occurs in rheumatic fever and other diseases. One has no right to say, because the patient has one disease, that a toxic eruption may not be due to some other cause. In other words, there is no evidence in this case to warrant the conclusion that the erythema multiforme is caused by a fungus.

DR. HERMAN GOODMAN: The lesions of the hands disclosed mycelia on two occasions. This is a rare finding. Thousands of patients with lesions of the hands are examined at the New York Skin and Cancer Hospital. In about three of each one hundred cases examined the reaction was positive. Dr. Williams claims about 1 per cent of positive findings in cases of lesions of the hands. It is

my practice to omit the examination of the hands and to restrict the examination to the feet. Positive findings in lesions of the feet are about 30 per cent of the total.

I think that the lesions on the body of the patient are toxic. I am interested in Dr. Cannon's idea. Does he maintain that dermatophytid is a proper diagnosis in this case if the patient has positive findings for ringworm on the palms and an eruption on the trunk that looks like erythema multiforme but from which one actually recovers fungi? Does his concept of dermatophytid include the presence of fungi in the lesion classed as dermatophytid? It is my impression that a dermatophytid is due to the toxins of the fungus and not to the fungus itself.

Is it impossible to have fungi on cutaneous lesions that are not caused by the fungi disclosed by the microscopic examination? Some years ago, a report from Washington was made on two patients with penile lesions in which fungi were found, yet these patients gave evidence of syphilitic chancres on the exact sites of the supposed tinea. This led me at the time to report a case seen in 1917. The patient had a clinical gumma of the forehead with a 4 plus Wassermann reaction. I found and cultured tinea fungi from the gumma. The lesion healed on administration of antisyphilitic treatment intravenously.

There are very few reports in the literature of positive human transplants of fungi cultures to normal skin. It seems possible that some of the ringworm of the skin may have the organisms adventitiously on some other cutaneous disease.

DR. HERMAN SHARLIT: At Beth Israel Hospital, from which this patient comes, are found many cases of fungus infection of the hands in women. This may be because the women at the clinic for cutaneous diseases are a group with a high diabetic incidence. The typical interdigital erosions of the hands are extremely common. We do not pretend to find fungi in any considerable proportion of the hands examined for fungi, but it is our impression that they are found more often than at other clinics, and this is because there are more patients with true fungus infection of the hands at this clinic.

DR. OSCAR LEVIN: I regard this case as one of dermatophytosis with trichophytids. Beth Israel Hospital, which is visited mainly by orthodox Jews, shows a high percentage of diabetic patients, and those who are not diabetic employ a diet high in carbohydrates. Because of the dietary laws, they do not use soap in washing dishes and the hands therefore become infected easily by yeast fungi and by other parasites. The trichophytids represent secondary reactions to the primary infections of the hands. This evening I presented numerous cases of tuberculosis. I wish to emphasize the multiplicity of the types of lesions which may occur in tuberculosis of the skin, as shown in these cases. Most of them represent different degrees of reaction of the skin to the tubercle bacillus invading the skin. Some lesions are lichenoid tuberculosis; others, papular tuberculids; others, lupus vulgaris, and still others, scrofuloderma. I believe that the same phenomena may occur in tinea infection, and that the parasites are carried to the skin from the primary focus to produce this type of reaction. The various eruptions represent different reactions, depending on the immunologic factors in the skin.

LUPUS MILIARIS DISSEMINATUS (?). Presented by DR. HERMANN FEIT.

J. M., a colored woman, aged 18, had had lesions for nine months. They had begun on the legs and elbows. Two months prior to presentation finer lesions, which were pruritic, had appeared on the neck and the eyelids. White spots had been present for two or three months on the legs. Two irregular patches about 3 by 1.5 cm. in size were seen on either side of the neck, containing small, discrete, shiny, flat-topped papules. There was some tendency to confluence. Similar lesions about the eyelids, the upper part of the chin, near the right elbow and on the anterior surface of both legs below the knees were present. Over the right sternoclavicular articulation was a linear band 2.5 cm. in length, of

similar papules, but with a more or less keloidal aspect. Scattered over the arms and legs were small, depigmented macules, the size of a finger nail. The Wassermann test was negative. The tuberculin test with old tuberculin 1 : 10,000 gave negative results. The histology showed a definite tuberculous structure, with necrosis.

HYDROA VACCINIFORME. Presented by DR. PAUL GROSS.

J. S., aged 7 years, had had a similar eruption one year before presentation. During the year prior to presentation the hands, forearms, legs and face had become involved. No similar eruption had occurred in other members of the family. On the forehead and cheeks an eruption of vesicles in three different stages could be seen. The earliest lesions were round and translucent; older lesions showed distinct, brownish centers. Still older lesions showed depressed brownish crusts surrounded by a formation of vesicles. There were numerous varioliform scars on the cheeks and arms. The legs and feet had similar scars. The eruption appeared to be caused by exposure to sunlight.

LICHEN SCROFULOSORUM. Presented by DR. OSCAR LEVIN.

H. E., a colored boy, aged 5, born in the United States, had a generalized, follicular, papular eruption, varying from that of a pinpoint to that of a pinhead in size. On the chest and back the lesions were flat and shining, while on the extremities, abdomen, back and buttocks they were more elevated and scaly. On the arms and lumbar region they were more papular and scaly and showed small necrotic lesions. Scattered over the skin were also healed scars varying in size from that of a lentil to that of a pea. Diagnosis on biopsy was tuberculosis.

LICHEN SCROFULOSORUM AND PULMONARY TUBERCULOSIS. Presented by DR. OSCAR LEVIN.

J. G., a white boy, aged 3, born in the United States, entered the Sea View Hospital with a diagnosis of hilar tuberculosis, tuberculous adenitis and dactylitis three years prior to presentation. On the posterior part of both shoulders there were shiny, flat-topped papules the size of a pinhead. On the middle of the neck there was a circinate patch consisting of firm, minute, scaly, shiny papules. On the forearm, the calves of both legs, the thighs and the lower part of the back there were a few pigmented scars the size of a lentil. The patient received general and local ultraviolet irradiation. The lesions healed with the development of superficial, slightly depressed and pigmented spots. The urine was normal, and the Wassermann reaction, negative. A culture from the throat was negative for diphtheria. The Pirquet test was negative.

VON RECKLINGHAUSEN'S DISEASE AND PULMONARY TUBERCULOSIS. Presented by DR. OSCAR LEVIN.

K. R., a colored woman, aged 25, married, born in the United States, had a caseous pneumonic tuberculosis. Pneumothorax had been performed. The cutaneous condition had been present for twenty-five years. The skin showed a generalized eruption made up of sessile, pedunculated, soft and harder papules and growths varying in size from that of a pinhead to that of a tangerine, and scattered freckles and larger patches of pigmentation. There was a large, pendulous tumor, the size of a tangerine, on the right arm.

Roentgen examination of the left shoulder showed three small localized areas of atrophy in the region of the greater tuberosity. The right shoulder showed a few small localized areas of atrophy in the region of the greater tuberosity. The wrists and hands were normal. The feet showed no abnormal findings, except prominent scaphoid bones. The skull showed a fairly large calcareous shadow in the frontal region. The dorsal spine was normal.

Urinalysis did not show acid-fast bacilli, but there was a faint trace of albumin. The Wassermann test was negative. Chemical examination of the blood showed 75 per cent hemoglobin (Dare), 4,150,000 erythrocytes, 0.9 color index, 9,150 leukocytes, 5 per cent neutrophils (segmented forms, 59 per cent), 22 per cent lymphocytes, 7 per cent monocytes and 7 per cent eosinophils.

LICHEN SCROFULOSORUM AND SCROFULODERMA. Presented by DR. OSCAR LEVIN.

W. T., a colored boy, aged 10, born in the United States, had had lesions of two years' duration. In February, 1930, the patient had scrofulous ulcerations of the neck, face and under the chin, and fine, small infiltrations on the right side of the face, discharging seropurulent fluid mixed with caseous matter and blood. There were numerous puckered scars. On the back over the entire trunk and upper extremities were scattered minute, follicular, shiny papules, the size of a pinhead, covered with tiny scales, firm in consistency and flat-topped. The patient had received ultraviolet irradiation, and the lesions had improved. The Pirquet test was positive. A patch test with tuberculin was positive, with formation of papules and vesicles. The examination of the urine, as well as that of the sputum and lungs, and the Wassermann test gave negative results.

ERYTHEMA INDURATUM AND PULMONARY TUBERCULOSIS. Presented by DR. OSCAR LEVIN.

S. V., a white woman, aged 29, single, born in the United States, had lesions of two years' duration. Scattered over the lower half of both legs were about two dozen necrotic, infiltrated lesions, varying in size from that of a lentil to that of a five-cent piece, and irregular ulcers covered with crusts. On the posterior part of the left leg there was a dark-red, purplish, crusted area, the size of a half-dollar, in which were several ulcers. The condition had begun as red spots which had grown worse in the winter. The patient had been in the Sea View Hospital for nine years.

Roentgen examination showed advanced pulmonary tuberculosis. The results of examination of the sputum were always positive. The Wassermann test was negative. Examination of the urine showed a slight trace of albumin and an occasional granular cast.

Biopsy showed dense infiltration of lymphocytes, plasma cells and giant cells. There were some newly formed elements of vascular and connective tissue.

LUPUS VULGARIS AND LICHEN SCROFULOSORUM. Presented by DR. OSCAR LEVIN.

T. L., a colored woman, aged 20, born in the United States, single, had lesions of six years' duration. The face, with the exception of the chin and the lower part of the right side, was almost entirely covered by tumor formation. The patient showed marked edema, swelling, closure of the eyes and small and large, soft nodules, scars and crusts. Scattered over the entire area were innumerable discrete and confluent nodules. There was extensive destruction of the nose, with a great deal of scar formation and crusting. The lip was very much swollen, infiltrated and covered with nodules. Scattered over the trunk and extremities were innumerable follicular, acuminate, flat-topped papules and several puckered scars. On the back were several necrotic papules.

Inoculations into guinea-pigs in 1930 and 1931 gave positive reactions. The tuberculin test (1:10,000) was strongly positive. The Wassermann test was negative.

The patient was said to have improved on a salt-free diet. She had received injections of a gold preparation and tuberculin intravenously. Ultraviolet rays from a water-cooled mercury vapor arc in quartz, and pyrogallic acid had been applied locally. Roentgen examination of the lungs was negative.

LUPUS ERYTHEMATOSUS AND PULMONARY TUBERCULOSIS (LOCAL INJECTIONS OF A GOLD PREPARATION). Presented by Dr. Oscar Levin.

R. J., a white man, aged 40, married, born in the United States, a tailor, had lesions of eleven years' duration and chronic pulmonary tuberculosis since 1931, caseous pneumonic in type, of the right upper lobe. The left cheek showed a patch of lupus erythematosus 1 inch (2.5 cm.) in width and ¾ of an inch (1.9 cm.) in length of eleven years' duration. There were atrophy, adherent scales and violaceous color. The patient had received treatment with local injections of a gold preparation, ultraviolet radiation, radium and solid carbon dioxide. Examination of the sputum had been positive, but was negative at the time of presentation. The Wassermann test was negative.

HODGKIN'S DISEASE. Presented by DR. OSCAR LEVIN.

M. B., a man, aged 33, born in Russia, was seen five months prior to presentation, at which time he complained of generalized pruritus. There were numerous scratch marks, excoriations, papules and erythema and pigmentation present on the trunk and extremities. Two months later a nonproductive cough developed. which at the time was severe enough to produce vomiting, and there was a gradual loss of weight. Three months later enlarged lymphatic glands developed. There was a protruding orange-sized mass on the right side of the chest in the area between the third and fourth costal margins. The patient had persistent leukocytosis of about 15,000, with red blood cells, numbering 5,200,000 and a hemoglobin of 62 per cent. At one time the white cells numbered 27,000; the polymorphonuclears, 88 per cent, and the lymphocytes, 12 per cent. The Wassermann test was negative. The blood dextrose was 80 mg.; the nonprotein nitrogen, 32 mg., and the cholesterol, 150 mg. per hundred cubic centimeters. The urinalysis gave negative results. The spleen was not palpable. Gastro-intestinal examination also gave negative results. Roentgen examination revealed a lymphomatous tumor springing from the right lung. Biopsy of a gland of the neck showed tissue characteristic of Hodgkin's disease. The patient received deep roentgenotherapy for the mass in the chest; as a result the mass diminished markedly, and the pruritus practically disappeared.

PHILADELPHIA DERMATOLOGICAL SOCIETY

JACQUES P. GUEQUIERRE, M.D., *Secretary*

May 6, 1932

JACOB M. SCHILDKRAUT, M.D., *Presiding*

GRANULOMA ANNULARE. Presented by DR. J. M. SCHILDKRAUT.

A girl, aged 4 years, presented a ringed eruption on the anterior surface of the feet and legs, which had remained little changed since September, 1931, when she was first seen by the presenter. The eruption was irregularly ringed, fused and pinkish, and at places had an elevated border. She had received two and one-half erythema doses of roentgen rays, with little permanent improvement, although there had been remissions. She was presented for suggestions as to treatment.

DISCUSSION

DR. JOHN H. STOKES: I subscribe to the diagnosis of granuloma annulare. A biopsy, of course, would settle the diagnosis. As a rule, such cases have in my experience responded to persistent roentgen treatment. Once in a while, the

condition disappears without treatment and sometimes after the use of a strong resorcinol ointment. I should say that the prognosis is fairly good.

DR. S. S. GREENBAUM: I likewise agree with the diagnosis and am surprised that the lesions have not disappeared under irradiation with the roentgen rays. My last patient got well after receiving intravenous injections of a gold compound and sodium chloride in small doses. If the condition does not clear up with the medication suggested by Dr. Stokes, I would suggest the gold compound and sodium chloride.

DR. J. M. SCHILDKRAUT: What would you consider a safe dose of roentgen rays, Dr. Stokes?

DR. JOHN STOKES: I think up to four skin units. My experience has been that better results are obtained with larger doses, one-half skin unit at a time. The last case I had did not respond well, so that I think Dr. Greenbaum's suggestion certainly ought to be considered. I am more and more careful about using gold compounds; there are most disconcerting reactions to it. I should hesitate a little about giving this child gold therapy.

DR. V. C. GARNER: A year ago, I presented a case of granuloma annulare on the ankle of a boy which did not respond to two and one-half skin units of roentgen rays, and Dr. Schamberg advised more roentgen rays. After three more treatments the lesion completely involuted. I have seen the boy at intervals during the last nine months, and the patch has not returned.

SCLERODERMA. Presented by DR. R. V. GILMAN for DR. F. D. WEIDMAN.

E. C., a woman, aged 21, was shown at the October meeting of this Society by Dr. Weidman (ARCH. DERMAT. & SYPH. **25**:560 [March] 1932) with moderately advanced zosteriform scleroderma. She was presented again to illustrate the cessation in the inflammatory phase (the condition being no longer progressive) and also to show the diminution in pigment and sclerosing effect. The diffuse atrophy was still present; however, a perfect return to normal was not anticipated. Apparently, the fundamental excitant cause had ceased to operate, and an unequivocal neurogenous factor had been existing in this particular zosteriform type.

Since she was last shown, about four months ago she had been given oral doses of tincture of belladonna and daily massage. Physiologic tests were made from time to time for sensation and temperature changes.

DISCUSSION

DR. ROSE HIRSCHLER: Was any study made of the thyroid?

DR. R. L. GILMAN: The basal metabolic rate was normal.

TUBERCULOSIS VERRUCOSA CUTIS. Presented by DR. THOMAS BUTTERWORTH.

A man, aged 52, employed in the postmortem room of the Philadelphia General Hospital, presented an eruption on the hands, which, he said was of four months' duration. When he went to the clinic, to the service of Dr. J. V. Klauder, one month before presentation, he presented on the back of the right wrist a slightly elevated plaque about the size of a silver dollar. It presented a rough surface, with adherent horny scales and a distinctive purplish-red border, and was moderately tender. There were four smaller though similar lesions on the distal parts of the fingers. A biopsy specimen was taken from the lesion on the wrist. Dr. Weidman reported the specimen to be "tuberculosis verrucosa cutis with pseudoepitheliomatous hyperplasia." A piece of the same specimen of skin was ground up and injected into a rabbit. A tuberculin test subsequently proved to be negative, and cultures taken at the same time have likewise been negative.

A roentgenogram of the chest and an examination of the sputum failed to reveal evidence of pulmonary tuberculosis.

The patient was given soothing applications and two roentgen treatments, after which the surface of the lesions became smoother and the plaques less elevated.

The interesting features of the case were the multiplicity of the lesions and the fact that the condition occurred in an attendant in an autopsy room.

Microscopic sections were shown.

DISCUSSION

DR. ROSE HIRSCHLER: In the small biopsy of such a lesion one does not find many tubercle bacilli, not as many as one would find in a piece of leprosy tissue, for instance. So it is quite possible that a piece of such tissue macerated and injected into a guinea-pig might easily prove negative, although the actual clinical picture is that of tuberculosis cutis. I should think that it might be very interesting to take another biopsy specimen and put it through the same process, to see whether tubercle bacilli can be found. Was any of the tissue stained in such fashion as to find the bacilli in situ?

DR. T. BUTTERWORTH: Such a stain was not made.

CHROME ULCER. Presented by DR. D. PILLSBURY.

A man, aged 22, presented several chronic ulcers on the flexor and the extensor surfaces of the left wrist and on the third finger and thumb of the left hand. The ulcers were necrotic and had a very hard cartilaginous border. The lesions developed as follows: On Sept. 1, 1931, the patient, who is a jeweler and who had been working for six years, burned his wrist with sulphuric acid. The lesion healed slowly, taking about three months, during which time he continued to work. On Feb. 1, 1932, a phlegmatic ulcer developed on the flexor surface of the left wrist, which was excised by Dr. Ferguson of the University Hospital on February 13, and the lesion healed. On March 15, an ulcer on the extensor surface of the wrist developed, and since then the lesions appeared on the fingers.

The lesions have been uninfluenced by a number of treatments, including fractional doses of the roentgen rays and ultraviolet irradiation, and intravenous injections of thiosulphate and neoarsphenamine. The temperature of the skin was taken by Dr. Beerman of the University staff. It was practically normal, that of the left wrist being about one-half degree higher than that of the right. Normal fluid and wheal formation were obtained on both sides. The nasal septum was normal.

DISCUSSION

DR. V. C. GARNER: I have seen this patient once before, and I could not help feeling on the first examination as well as tonight that we have not completely eliminated a factitious eruption. These lesions appeared following a sulphuric acid burn. While the patient does not appear to be the type of person to do this, and Dr. Pillsbury assures me that the results of investigations have been negative, one cannot be sure.

DR. H. J. SMITH: I have seen chromic acid burns. While they are slow to heal, I hardly feel that they would be so slow as this one has been. Chromic acid is used to destroy tissue; under those conditions the ulceration formed heals rapidly.

DERMATITIS HERPETIFORMIS. Presented by DR. B. L. KAHN.

A. T., a white man, aged 37, was admitted to Dr. Maurice Brown's service in the skin ward of the Philadelphia General Hospital on April 11, 1932, with multiform lesions on the trunk, the scalp and the extremities, of four years' duration. The patient had been thoroughly studied at the Temple University Hospital and at the Skin and Cancer Hospital. Examinations were made of the blood and urine, and a biopsy was performed. He had received eighteen injections into the arm. He had also been given local remedies and a considerable amount

of roentgen therapy. The Wassermann reaction was negative. The sugar in the urine was a little more than normal. The outstanding features in the case were the multiformity of lesions, with grouping, and the intense itching, which suggest premycosis fungoides.

DISCUSSION

DR. J. P. GUEQUIERRE: We inherited this patient at Temple University Hospital at the time Dr. Wright took charge of the Dermatological Department. At that time he had an exfoliative dermatitis, and he gave a history of having had several attacks which cleared up when he was in the hospital only to recur when he returned home. Certain nervous and social factors were involved, we felt, in the situation at home that brought about a recurrence. The eruption cleared up completely while he was under our care, but as usual there was a fresh outbreak following his return home, and we advised admittance to the Philadelphia General Hospital.

I recall clearly Dr. Friedman's statement that the condition would most likely eventuate in mycosis fungoides. When the patient left the hospital, he did not look as he does today; he did not have the definite lesions. The question of dermatitis herpetiformis did not enter our minds at that time, but he gave a history of having received arsenical injections, which brought this about. The first attack was in April, 1929. He was treated briefly at that time for syphilis.

DR. JOHN H. STOKES: I have nothing much to add. I think it is a pity that so interesting a problem goes more or less by default in discussion. I think that the patient has a premycotic mycosis fungoides. That is only a tentative opinion. The scalp is too full of lesions for dermatitis herpetiformis, although the erythema multiforme type of dermatitis herpetiformis might present this type of lesion. I lean more toward a diagnosis of mycosis fungoides.

DR. R. FRIEDMAN: I recall this patient's having stated in his history that the eruption started about the genitalia. A physician prescribed an ointment, subsequent to the use of which a dermatitis developed. The patient received intravenous injections of a yellow-colored fluid, the exact nature of which could not be ascertained. It is probable that neoarsphenamine had been administered. At Temple University Hospital, he received numerous injections of sodium thiosulphate and local therapy. I believe he was admitted five times to the institution; each time a typical exfoliative dermatitis developed, which sometimes cleared up entirely and at others left violaceous, sharply marginated, markedly itchy, elevated plaques on the trunk and upper extremities. At no time were there bullous or vesicular lesions, although at times the plaques became moist and oozing. On each occasion when he was discharged from the hospital, the skin was perfectly clear. Within a few months, however, he would return with an exfoliative dermatitis and itching. We performed a number of biopsies and each report stated that exfoliative dermatitis was present. Prior to his transfer to the Philadelphia General Hospital last month two biopsies were made, one on sound skin and the other on one of the plaques. The uninvolved skin showed some thickening of the epiderm and mild inflammatory exudate in the corium. The report on the plaque was exfoliative dermatitis.

The blood picture immediately before the patient's transfer was perfectly normal, and all other laboratory investigations while he was at the hospital and also prior to his discharge showed normal results. The intense itching, the peculiar violaceous, sharply marginated plaques, the appearance and disappearance of the lesions and the peculiar course of the condition led us to make a tentative diagnosis of premycosis fungoides.

PSEUDOPELADE OF BROCQ. Presented by DR. V. C. GARNER.

I. C., a man, aged 33, an Italian, who had lived in this country for ten years, for the year preceding presentation had had an increasing number of patches of cicatricial alopecia of the scalp. The condition presented every classic earmark of the disease as outlined in the monograph by Photinus: multiplicity of lesions,

distribution over the vortex of the scalp, small size, spreading at the borders rather than circumscribed contour, cicatricial character and a little red subverticular flush around the roots of the involved hair. A great many of the hairs when removed showed a glassy bulb, a certain characteristic of this condition. The patient was also under the care of Dr. R. Friedman at Temple University Hospital, who performed a biopsy.

DISCUSSION

DR. R. FRIEDMAN: I agree with Dr. Garner's description of the physical and morphologic characteristics of the lesions which the patient shows on the scalp, but I should like to add that he has been under our observation at Dr. Wright's clinic for the last half year, and that we have followed the spread of some of these areas of alopecia closely. We have noted at the periphery of the cicatricial patches evidences of inflammation about the hair follicles. We made a diagnosis of folliculitis decalvans. The biopsy was performed late last week, and the report has not yet been received.

DR. S. S. GREENBAUM: In view of the history given by Dr. Friedman, I think it would be rather difficult to exclude folliculitis decalvans in this case and make a diagnosis of pseudopelade. There are several areas here that I think are likewise suggestive of lupus erythematosus. I do not see how differentiation could be made, except by following the case for several months in the way that Dr. Friedman has done.

TENTATIVE EPIDERMOLYSIS BULLOSA ACQUISITA. Presented by DR. V. C. GARNER.

A boy, aged 18, had had a recurrent dermatosis for four or five years, usually during midwinter and again during midsummer, the condition clearing up in the interim. The lesions for the most part existed over points of pressure, the elbows, the knees and the buttocks, and were small hemorrhagic vesicles which enlarged and produced erosive lesions, with underlined vesicular edges or at times rolled, indurated borders. The case had been studied elsewhere as well as in Philadelphia, and the laboratory data gave negative results, except that in one of the unruptured vesicles a hemolytic staphylococcus was found. The diagnosis suggested was only tentative. The condition arose when the patient was about 14 years of age. At presentation he showed multiple healing erosive lesions about the elbows and knees, and over various other areas of the body, particularly the buttocks, he had healed, scarred, atrophic, pigmented lesions of former attacks.

DISCUSSION

DR. JOHN H. STOKES: We offer epidermolysis bullosa as a tentative diagnosis. I have seen one case of acquired epidermolysis bullosa to which this case does not conform satisfactorily. The acquired form of this disease does not have seasonal onsets, the lesions do not extend in and of themselves, and they do not present indurated borders. What I would like to direct attention to is the localization of the lesions and the septic process at the sites, particularly on the extremities.

I have under my care at the present time a patient with a classic picture of erythema induratum of the Bazin type which strikingly exhibits this peculiarity. I should be inclined to believe that this patient is a victim of extreme allergy to an organism carried through the blood stream to sites of trauma rather than of epidermolysis bullosa. This boy is obviously in poor condition. The attacks are seasonal; there is an infectious background, and a cutaneous hyperallergic reaction to deposited organisms exists. I think that if we had the facilities and time to observe him just before the appearance of an outbreak and to make thorough systematic cultures of the blood, they might reveal something. The trouble is that all blood cultures are done after the actual dissemination of organisms, rather than before. I should not want the case to pass onto the records as

being authentically diagnosed epidermolysis bullosa acquisita, although we felt that that was a diagnosis we should offer since we could make no other.

DR. V. C. GARNER: Because we considered the case as septic, as Dr. Stokes suggested, we used neoarsphenamine. Following the second injection, the patient had a most violent nitritoid reaction, which lasted for practically an hour and demanded every effort in treatment.

HYPERTROPHIC LICHEN PLANUS OR PRURIGO NODULARIS. Presented by DR. S. V. KULCHAR for DR. JOHN H. STOKES.

A woman, aged 71, presented isolated, indolent, fleshy nodules over the arms and legs, varying in size from 0.75 to 1.5 cm., of fifteen years' duration. The surface of the nodules was finely mammillated with a small amount of punctate crusting, and there was some peripheral pigmentation. Over the legs were reticulated, infiltrated bands of hypertrophic skin in addition to the hypertrophic nodules. Healing was gradual, leaving an atrophic scar. The Wassermann test of the blood was negative. The lesions were accompanied by considerable itching.

DISCUSSION

DR. W. O. ROOP: I think that this is a case of prurigo nodularis rather than of hypertrophic lichen planus.

DR. R. GILMAN: I am inclined to think that it conforms to several cases of lichen planus that I have seen.

DR. S. S. GREENBAUM: I think that Dr. Hirschler should discuss this, as she described the first case of prurigo nodularis in America.

DR. ROSE HIRSCHLER: A case of "Multiple Tumors of the Skin Accompanied by Intense Pruritus" was described as such by Hardaway in 1880. Twenty-three years later, two almost identical cases were reported by Dr. Schamberg and me. This statement is in refutation of Dr. Greenbaum's remark.

The patient just presented by Dr. Kulchar strikingly resembles our patient in sex, chronicity of the condition, intense pruritus and location and multiplicity of the lesions, most of which are discrete, firm and noninflammatory. There is no extreme hyperkeratosis, which capped many of the lesions in our cases, and this patient has infiltrations in various areas not seen in ours.

It is this infiltration and the slight verrucosity over the lesions that suggest the diagnosis of hypertrophic lichen planus.

None of the patients with clearly defined cases of prurigo nodularis was helped by treatment, and tumors excised or scratched out recurred promptly.

Dr. Kulchar says the areas of atrophic scarring as seen in this woman are due to a slow healing of that part, which is very interesting but is not consistent with the original case descriptions.

It is my impression that this is a variant type of prurigo nodularis.

MULTIPLE XANTHOMAS. Presented by DR. G. V. KULCHAR for DR. JOHN H. STOKES.

A colored boy, aged 7 years, presented numerous grouped, firm, yellowish nodules varying from 0.5 to 1 cm. in diameter, over the arms, legs and buttocks and to a lesser extent over the abdomen, of six weeks' duration. Over the palms bilaterally were yellowish infiltrations extending along the palm lines. The boy had congenital syphilis, and previous to attending our dispensary had received five intravenous injections of neoarsphenamine, following which, in December, 1931, jaundice developed accompanied by constitutional symptoms. Since January, 1932, he has been under treatment exclusively with bismuth. The blood cholesterol was 379 mg. per hundred cubic centimeters, and the sugar, 112 mg.; the indirect van den Bergh test showed 2, and the direct test was negative.

DISCUSSION

DR. F. SUMMERILL: The pathologic section shows a picture more suggestive of keloid than of xanthoma, and it seems possible that such an abnormal formation of scar tissue might have resulted from the clearing up of inflammatory lesions as a result of therapy.

BROOKLYN DERMATOLOGICAL SOCIETY

A. M. PERSKY, M.D., *Secretary*

May 16, 1932

B. B. BERKOWITZ, M.D., *Presiding*

MACULAR ANESTHETIC LEPROSY. Presented by DR. W. H. BEST.

E. B., aged 30, a porter, came to this country from the Philippines seven years prior to presentation. He had been well up to three years before presentation, when numbness of the foot developed. This anesthesia progressed steadily, and soon a macular eruption was noted over the lower extremities and abdomen. Occasionally, he would complain of pains in the joints with intermittent swelling. The Wassermann reaction was 4 plus. Nasal smears were negative.

NODULAR LEPROSY. Presented by DR. W. H. BEST.

E. M., aged 29, married, a laborer, came to Brooklyn from the Virgin Isles, West Indies, eight years prior to presentation. There was no history of exposure to leprosy. The lesions were first noted on the nose and lips in 1928. He received roentgen treatments at the Skin and Cancer Hospital for several years. The lesions gradually spread over the whole face and both extremities. No anesthesia or paresthesia was present.

DISCUSSION ON CASES OF LEPROSY

DR. A. WALZER: What is the relation of the Wassermann reaction to leprosy? I understand that one of these patients had a 4 plus reaction and the other a 3 plus reaction. Some investigators claim that there are cases of leprosy with syphilis, and it is claimed by others that leprosy causes a positive Wassermann reaction. I think that the concensus is that a few cases of leprosy may give a positive Wassermann reaction, but that a positive Wassermann reaction in leprosy in the majority of cases means syphilis plus leprosy.

DR. W. H. BEST: It has been the experience of myself and my associates that a large percentage of cases of leprosy show a positive Wassermann reaction, and that in all these cases the history has invariably been negative for syphilis. I appreciate that this does not rule out syphilitic infection, but in some instances a suggestive history should be obtainable. It has been our experience that the Wassermann test is positive more constantly in the nodular type of leprosy and more rarely in the anesthetic type. So I should say that in the majority of cases leprosy is accompanied by a positive Wassermann reaction, although it may be intermittent, and that this positive Wassermann reaction is not due to a concomitant syphilis.

The anesthesia that develops at the site of the lesion is always secondary to the lesion; the smaller patches, or those of recent development, show little or no anesthesia. Not until the patch spreads by peripheral extension and is fairly well developed does the lesion produce the typical anesthesia. However, there is an anesthesia that develops in the extremities (the fingers and toes) in anesthetic types of leprosy that does not occur at the site of any cutaneous lesion. A history

will sometimes be obtained, as it was in this case, that even before the development of any lesions was noticed, a numbness of the fingers was felt. I had a similar case several years ago in a Japanese patient. He was a chauffeur, and the first thing he noticed was that his hands felt numb when he was driving the automobile. I saw him at the time that he noticed this numbness, and it was six or eight months before any cutaneous lesions developed.

In some cases of neuroleprosy, this numbness is the earliest manifestation of the disease, while in others the macular cutaneous lesions develop first, anesthesia occurring later.

A Case for Diagnosis. Presented by Dr. E. A. Gauvain.

E. T., a Negro boy, aged 15, born in Maryland and living there until two years before presentation, had scattered papular lesions on the face, torso and upper extremities of one and one-half years' duration. These lesions were shotty, flat-topped and about half the size of a pea, many of them appearing to have a slightly yellow color. They first appeared on the lips, in which location there was coalescence of several of the papules into a group. There were no subjective symptoms. The first lesions appeared shortly after the patient was vaccinated, at which time his lips were greatly swollen, but nothing further was known of the condition.

The report on the biopsy was "The sections show fused proliferative nodules just beneath the epidermis. In some respects they look like fused tubercles, but contain no giant cells. No large fatty or lipoid-containing cells are present. Similar nodules occur in the margins of chronic acne lesions." No diagnosis was made.

DISCUSSION

Dr. W. H. Best: The eruption is an old one and I cannot classify it. It suggests, in my opinion, multiple benign cystic epithelioma, for the lesions are rather soft. The lesions also suggest molluscum contagiosum, but I was unable to squeeze out any secretion.

Dr. A. Walzer: The first impression is one of molluscum, but after a more careful examination one finds that the lesions are follicular. The depression is really the opening of a follicle, and on squeezing one finds fluid, not a molluscum body. There were some lesions on the roof of the mouth. All in all, I think that the eruption is some productive process of the ducts of the oil or sweat glands.

Multiple Benign Tumor-Like Growths of Schweninger and Buzzi. Presented by Dr. E. A. Gauvain.

F. G., a woman, aged 49, married, born in Poland, had had the lesions for which she was presented for eighteen years. On both upper extremities there were numerous circular tumor-like masses, varying in size from that of the little finger-nail to that of the thumb-nail, round or oval, which on pressure disappeared and permitted the examining finger to pass into a depression bordered by a firm ring. There were also atrophic spots where old lesions had resolved. These lesions never gave any symptoms, subjectively, and the patient said that no new lesions had appeared. The patient could not describe the course of the lesions, but stated that when they were first noticed by her they were in the same condition as at the time of presentation.

DISCUSSION

Dr. A. Walzer: The whole process is a case of atrophy of the skin. The patient shows a definite acrodermatitis chronica atrophicans, with the beginning erythematous stages on both upper extremities, together with the macular atrophic patches.

Dr. E. A. Gauvain: These lesions began eighteen years ago. I questioned the patient rather closely in regard to the onset, and she said that they developed suddenly. They were the same size and just exactly as they are now. We saw

the atrophic spots of apparently recovered lesions that we know are found in this type of condition. She says that no new lesions have developed in eighteen years. I rather doubt that. About one year ago she had arthritis, and was first seen in the medical clinic. The internists attributed the edema and discoloration on her hands and arms to the arthritic process.

SCLERODACTYLIA. Presented by DR. L. J. FRANK.

D. S., a housewife, noticed a gradual contraction of the fingers about twenty years prior to presentation. First they became partly flexed on the palm, and then finger after finger shriveled and their ends began to drop off. The fingers became smaller and smaller. This process occupied about fifteen or twenty years. Her hands had been useless during the last six years. She said that she had never had a rash or ulceration.

Roentgenograms of the hands and feet on May 18, 1932, showed absence of the greater part of the distal phalanx of the thumb and of the terminal phalanges of the index and middle fingers, with abnormal contractures indicating trophic destruction. There were also ankylosis and deformity of the bases of the second and third metacarpals of the right hand, as well as absence of the fifth metacarpals on the right side and marked osteoporosis of the toes of both feet.

The Wassermann reaction of the blood was negative, and the urine was normal.

DISCUSSION

DR. S. HECHT: I believe that the patient has syphilis.

DR. W. H. BEST: The patient was admitted to the Kings County Hospital about ten days before presentation, because she wished to avoid having the toes get into the same condition as the hands. The diagnosis of sclerodactylia was made, with early involvement of the toes.

The diagnosis of syphilis is a rather hazardous one to make in the face of a negative Wassermann test. Dr. Hecht himself admits that in his vast experience with neurosyphilis, he has never seen so much bony destruction as this patient has. The clinical condition that she presents meets all the qualifications of sclerodactylia, irrespective of any syphilitic infection.

BRONX DERMATOLOGICAL SOCIETY

THEODORE ROSENTHAL, M.D., *Secretary*

Regular Meeting, May 19, 1932

HENRY SILVER, M.D., *President*

PURPURA WITH UNUSUAL FEATURES. Presented by DR. HENRY SILVER.

S. L., 51 years old, a business man, gave an irrelevant family and personal history.

The rash present appeared suddenly three months ago, and it was accompanied by pains in the shoulder joints and back. At the time of the onset there was no rise in temperature, and the patient was able to attend to his business. I saw him first two days after the outbreak, and the eruption then resembled erythema multiforme, but a few lesions showed capillary bleeding. A complete examination of the blood revealed no abnormalities. One week later all the lesions were purpuric. During the past three months some of the lesions have faded, leaving pigmentation; others have become deeper red and the whole has assumed a mottled appearance.

The primary lesion was a tiny papule, with a distinct deep brick red color. The lesions have enlarged peripherally, forming dime-sized plaques, which are soft. The surface of these patches is slightly wrinkled; some show telangiectasia. The color is cherry red, and the markings of the skin are accentuated. The entire appearance is bizarre because of the multiform character of the eruption. There are papules, round or oval plaques, annular lesions, scaly papules and large ecchymotic areas, but no vesicles.

The symmetrical arrangement of the eruption is striking. A dense crop of lesions is seen on the back of the hands and fingers up to the wrists, the rest of the extensor surface of the arms being entirely free from eruption. On the hands papular and annular lesions predominate. On the flexor surface and on the upper part of the arms, the ulnar side is mainly involved. Here the lesions are sharply defined, diffuse and brownish, enclosing normal skin between them. Around the elbows the lesions are papular and scaly. The lower extremities show the same striking symmetrical arrangement. The flexor and extensor surfaces are alike involved. The buttocks, knees and backs of the feet show the greatest number of lesions. In color and character the lesions are similar to those on the upper extremities.

A second study of the blood revealed: hemoglobin, 102 per cent; red blood cells, 5,120,000; white blood cells, 5,400; platelets, 240,000; polymorphonuclear neutrophils (segmented) 55 per cent; polymorphonuclear neutrophils (eosinophilic, 2 per cent; lymphocytes, 38 per cent, and monocytes, 5 per cent). There were 2 per cent reticulocytes; the bleeding time was one and one-quarter minutes and the clotting time eight minutes; the tourniquet test was positive, and the clot retraction time was two and one-half hours.

The Wassermann test of the blood and tests of the urine gave negative results.

Biopsy showed a thinned epidermis. The rete pegs were disturbed by edema which extended into the epidermis. There was no vesication or parakeratosis, but a slight hyperkeratosis was present. There was no evidence of atrophy. The cellular infiltration was limited, and was composed largely of small and large connective tissue cells. The process could possibly be parapsoriasis.

DISCUSSION

DR. J. G. HOPKINS: This condition appears to me to have the characteristics of a toxic eruption. I believe that it belongs to the broad group of erythema multiforme with hemorrhages.

DR. E. W. ABRAMOWITZ: I am fortunate in having seen the slide showing the biopsy specimen of this case, and am surprised to find such a striking difference between the clinical and microscopic picture. There is some telangiectasia present. Perhaps parapsoriasis or poikiloderm of Civatte is developing.

DR. P. GROSS: The lesions are localized over the superficial veins, and there are some lesions that are infiltrated. Because of the distribution and changes, the possible development of Kaposi's sarcoma must be considered, and also, because of the distribution about the blood vessels, one must think of livedo racemosa.

DR. B. OCHS: I think that this patient will have parapsoriasis.

DR. L. CHARGIN: The development of this case of multiform erythema-like lesions hardly permits us to fit the condition into the picture of poikiloderma or Kaposi's sarcoma. It must be pointed out that the pathologist finds no evidence of erythema multiforme. The condition may develop into parapsoriasis of the lichenoid variety, but a toxic eruption seems the most likely diagnosis.

DR. H. SILVER: Poikiloderma Civatte is usually limited to the face and neck and shows more atrophy and telangiectasia, characteristics that this case does not demonstrate. I agree with Dr. Hopkins that this condition is erythema multiforme with a purpuric tendency. I am surprised that the biopsy should show changes simulating parapsoriasis. What the final outcome of the case will be is hard to prognosticate.

ACNE KELOID. Presented by DR. BENJAMIN OCHS.

Mr. R., 24 years old, has been under treatment for a different disease than that for which he is presented.

Over both sides of the nape of the neck a number of hard, prominent, pustular lesions are diffusely spread, which vary in size from that of a pinpoint to that of a lentil. On the top of the scalp similar lesions are present, some healing with atrophy.

DISCUSSION

DR. S. FELDMAN: To my mind the lesions on the scalp are not seborrheic, and I think the process on the scalp is acne necrotica. One must also consider folliculitis decalvans. The lesions on the neck are too soft for the condition to be acne keloid.

DR. L. CHARGIN: I believe this to be an unusual form of folliculitis which leaves scars; however, it is not folliculitis decalvans. The process on the back of the neck is similar to that on the scalp, and I do not think that the lesions are typical of acne keloid. I favor a diagnosis of an unusual type of acne varioliformis.

DR. G. SPINNER: The redness on the scalp is due to dermatitis caused by a white precipitate ointment which he has been using recently.

DR. C. LERNER: I also believe this condition to be acne varioliformis.

DR. B. OCHS: Acne varioliformis of five years' standing with treatment is unknown to me. There should have been some results after treatment with ammoniated mercury. Furthermore, there is no acne varioliformis on the forehead or nose, which speaks against that diagnosis. I still maintain my original diagnosis of acne keloid. The patient is receiving treatment with resorcinol ointment and ultraviolet radiation on the scalp.

PARAPSORIASIS EN PLAQUES (BROCQ). Presented by DR. BENJAMIN OCHS.

Miss N., 20 years of age, for many years has had a number of sharply circumscribed, somewhat scaly patches diffusely spread over the greater part of the body, the face, neck and hands being the only parts that were free from the disease. These lesions grew slowly by peripheral extension, with slightly adherent scales on a macular base. Some of the lesions are as large as an ordinary saucer.

Biopsy made at the Post-Graduate Hospital confirmed the clinical diagnosis of parapsoriasis en plaques. It showed a moderately edematous process of the upper cutis which extended into the epidermis. The papillary bodies had dilated vessels, and the rete pegs were elongated and thinned. There was cellular infiltration composed largely of round cells in the upper cutis. Granulation was present throughout.

DISCUSSION

DR. L. CHARGIN: This case presents an unusual amount of scaling for one of parapsoriasis of the Brocq variety, but this undoubtedly is due to ultraviolet therapy.

BILATERAL HERPES ZOSTER. Presented by DR. I. M. LASHINSKY.

P. L., a man, aged 50, born in Ireland, a laborer, was admitted to the hospital on Oct. 10, 1931, with a pulmonary abscess complicated by a tuberculous process of the upper lobe of the left lung.

The laboratory findings were as follows: The urine was normal. The Wassermann reaction of the blood was negative. The sputum was normal. Chemical examination of the blood showed urea nitrogen 13 mg., creatinine 1 mg., and sugar 94 mg. per hundred cubic centimeters.

While in the hospital the patient received two blood transfusions. On March 29, 1932, 500 cc. of whole blood was given by the Soresi method with no untoward reaction. On May 13, 1932, a second transfusion of 500 cc. of blood was given

by the same method. That night a temperature of 105 F. developed, which gradually subsided, and on May 16, 1932, the eruption appeared.

The patient presented white vesicles varying in size from that of a pinhead to that of a millet seed on an erythematous base. The eruption appeared on an area supplied by the second cervical to the seventh cervical nerves and was about 5 cm. in width. The vesicles were closely grouped. The posterior areas of both auricles were covered with the same lesions. There was no pain preceding the eruption.

DISCUSSION

DR. L. CHARGIN: I favor a diagnosis of herpes simplex in this case. Bilateral herpes zoster is extremely rare. This condition lacks some of the characteristics of herpes zoster.

DR. E. W. ABRAMOWITZ: I agree with Dr. Chargin. In bilateral herpes zoster the condition is not symmetrical. In this case, furthermore, there is absence of pain. I favor the diagnosis of herpes simplex.

DR. J. G. HOPKINS: I advise animal inoculation. Herpes simplex could be reproduced but not herpes zoster.

DR. P. GROSS: From the clinical picture, the condition is herpes simplex. It does not have any particular nerve distribution. Animal inoculations would aid in the differential diagnosis.

DR. C. H. MARTIN: I favor the diagnosis of herpes simplex as against herpes zoster because of the symmetry of the lesions, the lack of pain and the superficial character of the vesicles.

DR. C. LERNER: I should like to know if the blood donor in this case had suffered several months ago from varicella. I ask this because of the relationship between varicella and herpes.

DR. S. FELDMAN: With respect to the remarks of Dr. Martin, the lesions of herpes zoster do not have to be large.

DR. I. M. LASHINSKY: To my knowledge, the donor did not suffer from varicella or herpes zoster at the time the transfusion was given.

A CASE FOR DIAGNOSIS. Presented by DR. MAX KAMPF.

Miss D. P., 23 years old, presents an eruption of eight months' duration, which is localized on the scalp, face, trunk and upper and lower extremities.

On the upper part of the body the lesions are predominately papular and are covered with a thick, whitish scale. Many of the lesions on the scalp are without scales and present a flattened, reddish and smooth surface. The character of the lesions on the lower extremities is entirely different. There they are grouped, raised considerably above the level of the skin, deep red and covered with thick crusts.

DISCUSSION

DR. S. FELDMAN: On the trunk the patient presents lesions that are psoriatic, and I believe psoriasis to be the diagnosis.

DR. C. GREENHOUSE: I believe this case to be one of exudative psoriasis. Perhaps the patient took some bromides which produced the fungating lesions on the lower extremities.

DR. P. GROSS: I think the condition is psoriasis and that the exudative lesions on the lower extremities are due to poor circulation. The patient has varicose veins, and they are the causative factor of the exudative psoriasis.

DR. L. CHARGIN: The most likely diagnosis is exudative psoriasis. One must, however, rule out syphilis.

DR. M. KAMPF: The Wassermann test was negative. Because of the unusual lesions on the legs my associates and I were afraid to venture a diagnosis of psoriasis. The lesions on the face and scalp originally impressed us as seborrhea.

TERTIARY SYPHILIS. Presented by DR. THEODORE ROSENTHAL.

Mrs. J. G., aged 47, married, has suffered from painful lumps on the sole of the right foot for the past six months. Twelve years ago she received some intramuscular injections for a "disease" she was said to have contracted from her first husband, from whom she was subsequently divorced.

On the sole of the right foot, on the inner aspect, are a number of subcutaneous pea-sized, purplish or bluish nodules, which are fairly firm, arranged in a serpiginous outline. Nearer the heel are two crusted atrophic areas, which according to the patient developed from the nodules. There are no lesions elsewhere.

The Wassermann reaction of the blood was 4 plus.

DISCUSSION

DR. S. FELDMAN: It is rather unusual for a tertiary lesion to persist for six months without ulceration. I suggest a therapeutic test.

DR. C. LERNER: If after antisyphilitic treatment, the lesion fails to clear, I should make a diagnosis of Kaposi's disease.

DR. T. ROSENTHAL: I do not believe that the lack of ulceration should influence the diagnosis in this case. The patient has two atrophic areas near the heel which are the remains of nodular lesions. Already, after one injection of bismuth, the lesions look a little better.

ERYTHEMA PERSTANS (?). Presented by DR. I. MOGIL.

The patient is a woman, 59 years old, married.

The eruption, which is of 3 months' duration, began on the lower extremities with large pea-sized, bright pink, solid papules or nodules. These later developed into large erythematous patches of various forms; some were circular or semicircular lesions with clear centers or broken up marginated segments. A new crop of lesions has appeared within the past week on the upper extremities, with a tendency to spread all over the body. They began in the same manner and developed into the same forms as those on the lower extremities.

Physical examination revealed a very anemic patient. Arthritis of both knees has been present for the last two years.

The Wassermann test of the blood was negative. The blood count showed: hemoglobin, 72 per cent; red blood cells, 3,210,000; white blood cells, 4,200; polymorphonuclears, 70 per cent; lymphocytes, 28 per cent; monocytes, 1 per cent, and eosinophils, 1 per cent.

DISCUSSION

DR. E. ABRAMOWITZ: This patient has lesions such as are usually seen in erythema multiforme. The term erythema perstans is no longer used; originally it referred to early lupus erythematosus. This eruption might be due to rheumatism, or to drugs, such as salicylates or cinchophen.

DR. I. MOGIL: This woman has suffered from arthritis for the past two years. She has been taking a variety of drugs over long periods.

BASAL-CELL EPITHELIOMA. Presented by DR. LOUIS CHARGIN.

R. T., 20 years old, single, a stenographer, about six months ago scratched the back of her left finger with a ring. The erosion was small but did not heal. In a week or two she had to remove the ring because the area became swollen. She consulted a number of private physicians, visited several clinics and received treatment with ointments and roentgen therapy and two radium treatments. The lesion refused to heal and progressed rather slowly. She was first seen by me about two months ago. At that time she presented a shallow ulceration at the base of the dorsal aspect of the ring finger of the left hand. The base of the

ulceration showed a mild mucopurulent discharge; the borders were undermined, and the surrounding area was acutely inflamed. There was no adenitis. The smears and the cultures proved negative.

The Wassermann test of the blood was negative on two occasions.

Biopsy revealed a basal cell epithelioma.

DISCUSSION

DR. B. OCHS: This case demonstrates the extreme value of a biopsy. My first impression of the lesion is that it was a tuberculoma.

DR. J. G. HOPKINS: I have never seen a basal cell epithelioma on the hand before, and should like to inquire whether any one present has seen such a case.

DR. C. LERNER: Dr. Eller presented a case at the Academy of Medicine about five years ago. It was believed at first to be one of sarcoid, but all those present were greatly surprised to find on biopsy that the growth was a basal cell epithelioma.

DR. W. SACHS: I should like to point out that several months ago I presented a similar case before this society.

DR. E. W. ABRAMOWITZ: I saw this woman about two months ago. She was then receiving roentgen therapy. I thought that the condition was dermatitis artefacta and am surprised to learn that it is a basal cell epithelioma. I suggest wide excision with the endothermy knife.

A CASE FOR DIAGNOSIS (ERYTHEMA MULTIFORME?). Presented by DR. I. M. LASHINSKY.

J. A. is 32 years of age, single, a Filipino, a cook.

Physical examination apparently gave negative results, save for the absence of eyebrows. The patient stated that about one year ago his head became entirely bald, but subsequently the hair gradually grew back.

He presents violaceous, discrete, infiltrated papules from the size of a pinhead to that of a pea and larger which are not pruriginous. The violaceous color of the papules has gradually become a shade paler toward the periphery. Some of these papules present a tiny central depression. On the dorsum of the left hand there is a silver dollar-sized circinate lesion composed of the papules just described.

The trunk and the extremities are covered with a diffuse, macular pigmented eruption ranging in size from that of a millet seed to that of a small pea. Some of these pigmented macules show pinhead atrophy in the center.

The patient stated that these pigmented macules were the result of lesions simulating those on the dorsa of his hands. The present lesions have lasted for about five months. They began to involute, however, after he had applied tincture of iodine for about two weeks.

The mucous membranes are absolutely free from the eruption. The epitrochlear glands are palpable. The Wassermann reaction of the blood was four plus. The urine was normal.

A biopsy specimen taken from a fresh lesion and examined by Dr. S. Peck showed that the main changes were in the cutis. They consisted of a marked edema with vascular dilatation and perivascular infiltration. The changes were limited to the papillary and subpapillary layers of the cutis, although the middle layer of the cutis was moderately involved. There was, in addition, subepidermal formation of vesicles. The epidermis showed practically no changes. In some places, epidermal edema was seen. This picture fits in with that of erythema multiforme.

DISCUSSION

DR. L. CHARGIN: It has been difficult to establish a diagnosis in this case. When the patient was first seen, the clinical appearance suggested erythema multiforme. There were numerous dime-sized, bluish-red lesions on the backs

of the hands. These, with the history of the acute onset, favored a diagnosis of erythema multiforme, but the pigmented lesions on the body, some of which showed atrophy, caused leprosy and leukemia to be considered. Even after the Wassermann test was reported positive, the case was not considered as one of syphilis. Since the administration of antisyphilitic therapy, however, the process has involuted markedly; hence the most probable diagnosis is syphilis.

DR. H. SILVER: It is odd that one should consider in the differential diagnosis diseases so far apart as erythema multiforme and leprosy. The reason for the consideration of leprosy is the absence of hair in the region of the eyebrows, the pigmentation and the atrophy. The case is evidently not one of leprosy. Syphilis simulating erythema multiforme is the likely diagnosis.

A CASE FOR DIAGNOSIS. Presented by DR. THEODORE ROSENTHAL.

G. R., a school boy, aged 15, born in Santo Domingo, who has lived in the United States for the past four years, presents an eruption of two months' duration.

On the extensor surfaces of the arms and legs and on the back are numerous discrete and confluent reddish papules. Some of the lesions have scaly caps; others appear umbilicated. On the arms there are faintly pigmented macular lesions which appear to be remnants of former active papulofollicular lesions. On the legs, interspersed among the active lesions, are large, pigmented, atrophic lesions the size of a split pea.

There are no lesions on the chest or the abdomen. On the face there are a moderate number of acneform papules and pustules.

DISCUSSION

DR. P. GROSS: I cannot offer a definite diagnosis in this case. The condition is a lichenoid eruption, which may be lichen planus. There is a tendency to grouping of the lesions.

DR. E. W. ABRAMOWITZ: I do not believe that the lesions are lichenoid. After ruling out lichen scrofulosorum, I think that this condition is ordinary eczema, especially after seeing the small lesions on the penis.

DR. S. FELDMAN: This case impresses me as being one of allergic dermatitis.

DR. L. CHARGIN: My first diagnosis in this case is syphilis, and the second, tuberculosis. I believe that dermatitis of external origin can be ruled out. The grouping of the lesions in this case suggests syphilis. This type of syphilis is frequently seen in association with iritis.

DR. E. W. ABRAMOWITZ: Are there any corymbiform lesions?

DR. L. CHARGIN: There are no corymbiform lesions.

DR. T. ROSENTHAL: I believe that the lesions are definitely lichenoid, either tuberculous or syphilitic. In the right clavicular region is a group of skin-colored folliculopapular lesions resembling those seen in lichen scrofulosorum. On the other hand, the grouping of the lesions on the back is strongly suggestive of a corymbiform arrangement. The Wassermann reaction of the blood will be reported in a day or two.

NOTE.—The Wassermann and Kahn tests were reported 4 plus the next day.

POLYCYTHEMIA. Presented by DR. HARRY B. FEILER.

H. R., a man, 55 years of age, noticed that since 1927 the color of his face and hands had assumed a bluish-red hue. He was a waiter and stated that up to 1927 he was in good physical condition. Since that time he has had hematuria and frequency of urination.

The dorsal aspects of both hands and the face are bluish red; the palmar aspects of the hands are brick red. The discoloration of the hands extends up to the lower third of both forearms.

The blood count showed: hemoglobin, 110 per cent; red blood cells, 9,000,000; white blood cells, 8,600; polymorphonuclears, 70 per cent; lymphocytes, 28 per cent, and monocytes, 2 per cent.

DISCUSSION

DR. I. M. LASHINSKY: I believe that the tongue undergoes changes in polycythemia. Has this patient any lesions of the tongue?

DR. J. G. HOPKINS: The patient exhibits acromegalic characteristics with marked prognathism. It would be interesting to secure a roentgenogram of the sella turcica.

DR. H. B. FEILER: The patient has not presented any lesions on the tongue.

SECONDARY SYPHILIS. Presented by DR. THEODORE ROSENTHAL.

I. W., born in China, who has lived for eighteen years in the United States, had a sore on the penis ten months ago followed by a generalized eruption at that time. He received ten intravenous injections of arsphenamine.

The present eruption appeared several weeks ago and is localized on the back of the neck and the face, wrists and palms. On the back of the neck the eruption consists of several erythematous flat papules the size of a dime with a pigmented center, some isolated, some arranged in circles. On the chin and around the lips are numerous tiny papules; two lesions are distinctly annular. On the left palm, large reddish maculopapular lesions are present.

The Wassermann test of the blood was negative.

DISCUSSION

DR. S. FELDMAN: While syphilis may imitate any condition, the lesions on the back of the neck do not appear to fall into that category.

DR. T. ROSENTHAL: It is true that the lesions on the back of the neck are not typical, as the pigmented center and papular border would suggest possibly a lichenoid eruption, but the annular lesion on the chin, with the maculopapular lesions on the wrists and palms, makes the diagnosis of syphilis certain.

SAN FRANCISCO DERMATOLOGICAL ASSOCIATION

JOHN M. GRAVES, M.D., *Secretary*

May 20, 1932

CHARLES E. SCHOFF, M.D., *Chairman*

A CASE FOR DIAGNOSIS. Presented by CHARLES E. SCHOFF.

W. T., aged 41, a Greek, presents lesions on the lower parts of the legs between the knees and ankles, involving the entire cutaneous surface. The lesions are small, shotlike, about the size of a no. 8 bird shot, discrete, slightly depressed at the summit and interfollicularly placed. None were found to be pierced by a hair. They are dirty brownish, with no erythema and slight itching. There are no other similar lesions on the body. The lesions are of one year's duration. There is no adenopathy. The white blood cells, on April 19, 1932, numbered 16,000. The differential count showed: lymphocytes, 15 per cent; eosinophils, 1 per cent; mononuclears, 10 per cent, and polymorphonuclears, 74 per cent.

The past history revealed that a diagnosis of "scrofula" was made in Athens in 1924; the patient responded to roentgen treatment. The Wassermann test was negative in 1920. Lipomas (small) were removed from the neck. In February,

1930, a roentgenogram of the chest was normal, and examination of the sputum gave negative results. In October, 1931, roentgen examination of the chest gave negative results.

DISCUSSION

DR. C. E. SCHOFF: This man has a history of glandular enlargement from time to time. I thought of leukemia and also of lichen planus, but the biopsy did not help in the diagnosis. It showed a chronic inflammatory condition of the skin with hyperkeratosis.

DR. L. R. TAUSSIG: The most striking feature shown in the section is the marked hyperkeratosis. The inflammatory reaction is slight. The condition is not lichen planus or Darier's disease, nor is it suggestive of leukemia.

DR. ERNEST CHIPMAN: Is it possible that the itching is due to some internal condition? The itching preceded this lesion, did it not? While the papules are definitely neoplastic, they do not resemble those of lichen planus.

DR. HOWARD MORROW: Clinically, I am inclined to believe that the condition is lichen planus; but if there is one clinical condition in which the diagnosis is definitely corroborated by microscopic examination, it is lichen planus. The sections should determine that. I should study the sections a little more closely.

MORPHEA. Presented by DR. C. J. LUNSFORD.

The patient, Miss G. L., aged 70, gave the following history: The lesion appeared as a white spot on the right cheek near the nose seven years ago. It gradually spread, until it is now 1 cm. in diameter. Inspection revealed a moderately indurated, well circumscribed, white or ivory-colored, flat lesion. The only subjective symptom was occasional mild itching. On the forearms were a few pinhead-sized white spots which were depigmented macules. There were no signs of atrophy. General physical examination otherwise gave negative results. Laboratory findings were normal, except for a basal metabolic rate of —16 per cent. The patient has been given 1 grain (0.06 Gm.) of thyroid daily. She is a native of Russia, but has been in the United States for seven years. About the time she came here, the lesion described developed on the right cheek near her nose. It was hard and indurated. She was seen in the clinic about six weeks ago. Biopsy was not requested. The lesion on the cheek has softened under thyroid medication during the past six weeks. There is no history of local injury, and there are no lesions in the mouth.

DISCUSSION

DR. H. E. ALDERSON: The condition looks more like morphea than any other condition. Yet it lacks some essential features of morphea. A biopsy would be desirable, but on the face it would be difficult to secure enough tissue.

DR. HOWARD MORROW: I think that the lesion is a nevus. Every two or three years one sees a lesion like this one—usually on the cheek, sometimes on the nose—which is indistinguishable from a basal plaque or a small patch of morphea. My associates and I have had four or five patients with this condition since we have learned to recognize it, and we have always wanted to secure a biopsy specimen. The lesions resemble a basal plaque, except for the fact that they have changed little over a period of many years. I think that this condition is a distinct clinical entity, although I have never seen it described.

I have never been cold-blooded enough to ask for a biopsy specimen; or I have not found women who were good-natured enough to give a specimen. The lesion is a nevus which develops before or after puberty, grows to a certain size and remains stationary all the rest of the patient's life. Dr. Taussig has seen two or three of these patients.

DR. MERLIN MAYNARD: I have been wondering what one does for patients with this condition. I have one patient now. I have used carbon dioxide snow. I have no doubt that the lesion is of the same type. My patient is a girl of 18.

The lesions grew to their present size in two years. They have remained stationary in size for the last eight or ten months. I thought that I might be able to smooth them out a little; so I used carbon dioxide snow.

DR. CHARLES SCHOFF: I wonder if one can attach any significance to the spots on the arm that developed in this case. I wonder whether there would be any relation between them and the lesion on the face.

DR. C. J. LUNSFORD: I think that I can get a biopsy specimen from this patient. If I do, I will send Dr. Morrow the slides.

COCCIDIOIDAL GRANULOMA. Presented by DR. N. N. EPSTEIN.

In a white woman, aged 74, a subcutaneous abscess developed on the left side of the neck in January, 1932. The patient had been an inmate of the Laguna Honda Relief Home for the year and a half previously. She had spent the greater part of her life in Tuolumne County (San Joaquin Valley), California, and had been a teacher. In later years she had lived in San Francisco and had made occasional visits to Tuolumne County.

The first lesion appeared as a subcutaneous mass which became reddened over its surface and broke, discharging pus. The resultant ulcer healed slowly in about four months. Two weeks prior to this presentation two new lesions appeared on the left side of the neck. The organisms of coccidioidal granuloma were demonstrated in microscopic sections.

DISCUSSION

DR. N. N. EPSTEIN: This case is very interesting. The patient was in an institution when the symptoms developed, showing an incubation period of at least one and one-half years. A mass developed on the left side of the neck which broke down and ulcerated and which was thought to be a punched-out syphilitic gumma. The presence of Coccidioides was not thought of at that time. A biopsy specimen was taken, and cultures were made at the same time. The presence of Coccidioides was reported on an examination of the sections. The culture did not grow. The incubation period in this case must be at least a year and a half. It has been that long since the patient has been in the territory where Coccidioides commonly is found.

At the Relief Home there are two patients with coccidioidal granuloma. In one case the diagnosis was made only by the pathologic picture. The diagnosis of coccidioidal granuloma is frequently made on the discovery of the presence of the organisms in the tissues. I do not know whether active treatment should be considered in this case, because of the patient's age.

The lungs are normal, except for one spot.

I should like to comment on the man shown here about six months ago with the lesion of coccidioidal granuloma on his hands. He died of acute heart failure, and autopsy showed Coccidioides in the lungs, as well as on the hands.

DR. H. E. ALDERSON: Is it not possible that this patient contracted the coccidioidal infection from the other patient in the Relief Home who had it?

DR. N. N. EPSTEIN: The two wards where these patients are located are far apart, and there is no communication between the men's and the women's wards. I do not see how the infection could have been contracted in that way, except possibly through the roentgenologic rooms.

DR. HOWARD MORROW: No case of coccidioidal granuloma has ever been known to have been contracted from a patient. The infection is contracted in the course of laboratory investigations or in endemic areas.

DR. MERLIN MAYNARD: Dr. Dixon did not consider that the infection could not be transmitted.

DR. E. K. STRATTON: I should like to ask what stain is used in order to recognize the coccidioidal bodies, and whether the lesion over the sternum is a typical one.

DR. HOWARD MORROW: Coccidioidal organisms will take any stain—hematoxylin, gentian violet, etc. The lesion over the sternum is characteristic.

DR. H. E. ALDERSON: I should like to know what to do for these patients. My associates and I have tried everything, but have had little success. One of the students at Leland Stanford University contracted the infection in the laboratory, and he recovered completely under treatment with antimony and potassium tartrate. Regarding the finding of organisms in small inconspicuous lesions, I wish to recall an interesting case in which Dr. Hiram Miller demonstrated organisms in scrapings from a tiny scaly lesion in the eyebrow.

DR. MERLIN MAYNARD: A sheep herder came in from the San Joaquin Valley with a lesion on the ankle. A diagnosis of coccidioidal granuloma was made. Within two weeks, the infection had extended to the knee. Coccidioides was constantly present in the sputum. The patient became very emaciated, and his condition rapidly grew worse. It appeared as though he could not live a month. He was given injections of antimony and potassium tartrate daily. Within a few days after the first injection the lesions began to heal. I saw the patient a month later, and he had gained from 15 to 20 pounds (6.8 to 9 Kg.) and was going back to work. To all appearances he is entirely well.

DR. J. M. GRAVES: I believe that one must not generalize too much. All the members of the society remember Dr. Miller's patient mentioned by Dr. Alderson. One leg was amputated many years ago because of coccidioidal granuloma. A year or two ago he was perfectly well, but came for consultation because of two chronic patches of dermatitis, each the size of a dime, one on the left upper lid and the other on the right temple. Dr. Miller was able to express serum from these lesions and to identify the organisms. The man had apparently established immunity.

CHICAGO DERMATOLOGICAL SOCIETY

E. A. OLIVER, M.D., *Secretary*

Annual Meeting, May 25, 1932

MICHAEL H. EBERT, M.D., *President, Presiding*

A CASE FOR DIAGNOSIS. Presented by DR. E. A. OLIVER and DR. PHILLIP GEYER.

A man, aged 63, first noticed a cutaneous eruption on the left anterior tibial surface five years before presentation. It remained as a localized patch for three months. Then the entire body was involved. He stated that early in the development of the lesions he noticed vesiculation and later desquamation. There were also periods of acute inflammation associated with severe pruritus and irritation. In the last few years the skin had undergone pigmentary changes, atrophy and wrinkling. About six months ago a lesion appeared on the upper part of the left thigh, which grew rapidly until at the time of the patient's admission to the hospital it was 3 cm. in diameter and extended about 1 cm. above the skin level. The central portion of the lesion was ulcerated, and the edges were rolled and rounded. On April 7, 1932, this lesion was excised for biopsy.

Examination revealed a poorly nourished, bedridden man. There was a symmetrical and widespread pigmentary eruption over the entire body, involving the entire surface of the skin except on the head and neck and the distal portions of the extremities. There was diffuse scattered atrophy of the skin, with associated wrinkling, and the skin was freely movable over the underlying fascia. A few areas of capillary hemorrhage were also seen. The pigmentary changes were of the diffuse erythematous type.

The Wassermann and Kahn tests were negative. Urinalysis gave negative results. Examination of the blood revealed 4,150,000 erythrocytes, 13,400 leukocytes and 78 per cent hemoglobin. The differential count showed: polymorphonuclears, 74 per cent; large mononuclears, 4 per cent; small mononuclears, 20 per cent, and eosinophils, 2 per cent.

Biopsy revealed no malignancy in the excised lesion.

DISCUSSION

DR. WILLIAM ALLEN PUSEY: I think that this condition is probably a secondary manifestation. The man had a senile skin to start with and might therefore have keratoses and perhaps epitheliomas. He has an extensive pigmentary process, which may be lichen planus, although I do not think that it is. It may be vagabondismus or something of that sort. As the man may have lived a hard life and may on some occasions have had pediculi, I think that some of the scars may be simply echthymatous scars.

DR. H. E. MICHELSON: It is difficult to discuss this case without having biopsy specimens from sections of the skin outside of the ulcers. I consider it likely that the condition is lichen planus, because there is a reteform eruption. Poikiloderma always comes to mind in any reteform eruption, but this eruption is not the color of poikiloderma. Some of the patches may be the lesions of morphea, but I cannot conceive of morphea resembling this condition. I have no diagnosis to offer.

DR. EDWARD A. OLIVER: To me this is a very interesting case. I disagree with Dr. Pusey in that I do not believe the man has had vagabond's disease. He came into the United States Veterans' Hospital to have a lesion on the thigh excised, and I saw him while he was under observation. No histologic study has as yet been made. My first thought was that the eruption was probably the result of arsenic. I have questioned the patient carefully, however, and can get no history of ingestion of arsenic. With the atrophy and the telangiectasia, in places the picture brings up the possibility of poikiloderma. I do not believe that the condition is poikiloderma, but I am at a loss to make a definite diagnosis.

DR. WILLIAM ALLEN PUSEY: I merely wished to mention vagabond's disease as one of the factors that may have caused the condition. There is a great deal of infiltration of the skin, but that may be chronic dermatitis persisting for a long time. The point I made was that I think the eruption is secondary to some of the conditions that have been suggested. I wish to say a word against the diagnosis of poikiloderma. I think this diagnosis is being overworked. Not much is known about the condition, and whenever one has a confusing case one thinks of that possibility.

DERMATITIS REPENS. Presented by DR. ARTHUR W. STILLIANS.

A boy, aged 9, was presented at the December, 1931, meeting of this society and is shown at this time in order to demonstrate the effect of treatment with yellow staphylococcus bacteriophage made by the Besredka method. He had been given forty or more intradermal injections of this stock preparation, twice weekly, first into the forearm and recently into the palm. Local wet dressings of saturated boric solution were used at first, and then 10 per cent boric acid in petrolatum was applied.

Examination showed the hand to be nearly free from dermatitis, only a portion of the palm still being involved. The thumb nail had not grown to the normal size; it extended only half way to the end of the thumb. On exposure to the air the patient complained of a drawing, unpleasantly dry sensation. No pustules had been present for some time.

DISCUSSION

DR. JAMES H. MITCHELL: When this boy was shown before, I mentioned that I had that day seen a case which I thought to be one of dermatitis repens.

The treatment consisted of nothing but potassium permanganate baths and treatment with ultraviolet rays from an air-cooled quartz mercury vapor arc lamp, and the patient is now practically well, which proves to me that I was mistaken in the diagnosis.

DR. ARTHUR W. STILLIANS: We are told that the bacterial antigen made by the method of Besredka is as much a bacteriophage as those made differently. My associates and I used a stock preparation.

DR. WILLIAM ALLEN PUSEY: This result of Dr. Stillians is very interesting. I too have seen a case in which the diagnosis could not have been questioned. The condition was cleared up with coal tar ointment.

DR. JAMES H. MITCHELL: I feel toward dermatitis repens about the same as toward pemphigus. If a patient gets well, the diagnosis is wrong.

DR. OLIVER S. ORMSBY: I have not seen a patient with dermatitis repens recover. Conditions resembling dermatitis repens that clear up are usually infectious dermatitis. I do not know how one can prove the diagnosis, but, as Dr. Mitchell said, patients with dermatitis repens do not get well.

DR. ARTHUR W. STILLIANS: We do not claim that the treatment used in this case is specific for dermatitis repens. We think that diagnosis justified because the boy has had the disease since he was 3 years old. Many other methods of treatment had been used, with no lasting effect.

A CASE FOR DIAGNOSIS (GRANULOMA PYOGENICUM?). Presented by DR. W. W. DUEMLING.

Dr. H. O. J., aged 50, first consulted me one week ago regarding a lesion on the hard palate. His past history was irrelevant. He stated that about three months ago he was suddenly aware of the fact that his mouth was filled with blood. On washing out his mouth, he could not determine the source of this hemorrhage. Since that time he had experienced brisk but short hemorrhages on numerous occasions, sometimes as often as once a day. Five weeks ago he first became aware of a small papule on the hard palate and he had been able to produce the hemorrhage by slight suction with the tongue on this papule or by slight trauma occasioned by eating. Otherwise the lesion had been entirely asymptomatic.

Examination revealed a lesion located on the hard palate just to the right of the median raphe. It presented as a small pea-sized, grayish papule which arose rather abruptly from the surrounding mucosa. The central portion was depressed and brownish red. To palpation the lesion was entirely soft and could be compressed against the hard palate. Roentgenologic studies gave negative results.

DISCUSSION

DR. H. E. MICHELSON: Clinically the diagnosis seems to me to be granuloma pyogenicum. There are the color and history of hemorrhage, and the lesion on the mucous membrane has flattened out and also is paler. If the condition is a sarcoma of three months' duration, of what type is it? It is not in the bone, for the roentgenograms are normal. If it were a round cell growth, it would be much larger within three months. I think that the lesion should be entirely removed with a cautery knife and examined under the microscope; then it would be known what it is. This may be done with little difficulty.

DR. W. W. DUEMLING: When I first saw this lesion it was my impression that it was either a pyogenic granuloma or an angioma, but as a diagnosis of sarcoma had previously been suggested to Dr. J., I urged him to come to this meeting and get the opinion of the members of the society.

NOTE.—The lesion was removed by electrocautery on June 3, 1932. Histologic examination revealed it to be a granuloma pyogenicum, and in looking over the sections, Dr. Udo J. Wile pointed out the striking resemblance in one

portion of the section to angiosarcoma. Several weeks later the patient returned with a small sequestrum which had come away from the hard palate in the area where the lesion had been, in the central portion of which there was a small splinter which could not be positively identified, but which looked like either a fish bone or a splinter of wood. It is possible that this foreign body was the etiologic factor in the production of the lesion.

A Case for Diagnosis (Pemphigus? Pityriasis Rosea?). Presented by Dr. Michael H. Ebert and Dr. Ruben Nomland.

A woman, aged 56, complained of sore mouth for about six months. It had been relieved temporarily for short periods. Within the three weeks prior to this presentation lesions had appeared on the abdomen.

Examination revealed many erosions of the mucous membrane of the roof of the mouth the size of a match head. There were several similar but larger eroded areas on the sides of the tongue. The gums were soft and spongy, and the breath was foul. On the abdomen were about a dozen dry, apparently scaling lesions. On one occasion one of these lesions was seen to be a small, noninflammatory, flaccid bulla. Subsequently numerous oval, erythematous, pruritic lesions developed on the body.

DISCUSSION

Dr. Michael H. Ebert: This condition has undergone a rather interesting transformation since I first saw the patient. She came to me with erosions on the tongue. There was no evidence of Vincent's angina, and the lesions were not of the type usually seen in multiform erythema. Only accidentally were the bullae discovered on the upper part of the abdomen. At this time the lesions on the body look like those of multiple erythema, but I still maintain that the lesions in the mouth do not resemble that disorder.

Dr. Clark W. Finnerud: I think that the eruption on the trunk is a form of toxic dermatitis, not necessarily connected with the condition in the mouth. The type of eruption seen on the trunk, even if untreated, commonly disappears within three or four weeks. I believe that one is too inclined to call many of these toxic eruptions pityriasis rosea, simply because they have a more or less self-limited course, and because some of the macular lesions of the trunk tend to clear in the center.

Dr. F. E. Senear: I think that the eruption on the trunk is distinct from that in the mouth, and that that on the trunk is pityriasis rosea. One has recently seen more cases of the inflammatory type of pityriasis rosea than usual, and there has been more extensive involvement of the face. Because of the parallel arrangement of the lesions, I think the condition is a mixed type of pityriasis rosea with vesicles, which are occasionally seen in that disorder. I do not know what to say about the lesions in the mouth.

Dr. William Allen Pusey: I am interested in Dr. Senear's remarks about pityriasis rosea. I had not thought of that diagnosis, but one of the lesions, now that I recall it, was suggestive of pityriasis rosea. That suggests that the woman has two conditions, the toxic erythema and also the lesions in the mouth, which were recently thought to be pemphigus. The lesions under the tongue gave me the impression that they might be those of pemphigus.

Dr. H. E. Michelson: Several years ago my associates and I made a number of biopsies in cases of pityriasis rosea, and I was struck with the intense inflammatory reaction. I do not understand why one does not see more bullae. Bullae have been described in pityriasis rosea (Blaschko: Arch. f. Dermat. u. Syph. **49**:383, 1899).

Dr. Clark W. Finnerud: I should like to mention a case I saw recently in which there was typical pityriasis rosea on the trunk, arms and thighs, associated with a marked vesicobullous eruption on the palms and soles. I have seen several such cases. Specimens have been uniformly negative for fungi. If the condition

in the case under discussion is a toxic eruption and not pityriasis rosea, as I believe to be the case, I am inclined to think that some of the eruptions which one is prone to call pityriasis rosea because of their tendency to clear in the center are not pityriasis rosea.

DR. CLEVELAND J. WHITE: When I was with Dr. Osborne I saw a case of active epidermomycosis of the feet from which fungi were recovered and which was accompanied by a typical pityriasis rosea-like eruption of the chest.

DR. F. E. SENEAR: About three months ago I had exactly the condition that Dr. Finnerud described, an eruption typical of pityriasis rosea on the trunk. Several men saw it and considered it typical, and a few days later a vesicular eruption developed on the hands and feet, followed by complete exfoliation, the picture then being that of a toxic erythema. I think that one sees many pityriasis rosea-like eruptions which prove not to be that disorder. In my case the condition on the trunk cleared up in a week but that on the hands and soles took somewhat longer. I think that this case will show more definite characteristics in a week or two.

EPIDERMOLYSIS BULLOSA CONGENITA. Presented by DR. JAMES H. MITCHELL.

A girl, aged 15, was one of twin sisters. The other twin was well and strong, with no cutaneous pathologic condition. One brother, aged 10, had no cutaneous lesions. Her father and mother were living and well, and there was no history of a similar case in her parents' families. The Wassermann reaction had been repeatedly negative with serums of the entire family. The patient was born six weeks prematurely and was delivered with forceps before her sister. There was forceps trauma on the right side of the forehead. Vesicles on the palms and soles were seen at delivery and were thought to be traumatic. She was unable to nurse for the first month, and was fed with a spoon. Her gain in weight was slow, whereas her sister gained rapidly. Lesions continued to form in increasing numbers and size, accompanied by marked pruritus. The palms and soles had been most markedly involved. The patient had learned to use the dorsa of her hands instead of the palmar surfaces, and as a result large keratoses had developed over the joints. When bullae were ruptured they healed promptly. The patient had been unable to wear any constricting articles of clothing, such as garters or elastic in bloomers. Walking was almost impossible. As a result, the muscles of the legs were atrophied, and the patient was able to put her feet behind her neck with ease.

Treatment had been varied and intensive. She had received innumerable exposures to roentgen and violet radiation. Stock and autogenous vaccines had been employed, with sharp reactions; intravenous injections of iodine cacodylate and neoarsphenamine, inunctions of mercurial ointment and mercury administered internally were given until the kidneys were damaged. The liver had become enlarged. "Gallons of arsenic" had been injected.

The patient was cheerful and, despite her handicap, had been able to keep her place in school, notwithstanding the fact that she started at 9 years of age.

On examination, the urine was acid, with from 4 to 8 pus cells to the field and no albumin or sugar.

DISCUSSION

DR. JAMES H. MITCHELL: The young physician who referred this patient to me hoped that there would be some therapeutic suggestions. Regarding classification, the condition is not hereditary, because no other member of the family is affected. Regarding the dystrophic form, the nails have been normal, except for secondary changes, and the hair has been normal. The general health of the patient has been excellent. There is a definite history of traumatic vesication.

ACRODERMATOSIS CHRONICA ATROPHICANS. Presented by DR. F. E. SENEAR and DR. MAX S. WIEN.

A. A., a white woman, aged 69, from the University of Illinois, was in good health until three years ago, when she began to have severe pains in the legs on

standing and persistent itching of the forearms and legs. When scratched, these areas became erythematous and crusted, and the condition persisted with remissions at intervals of from one to two months. For the three weeks prior to this presentation there had been involvement of both thighs with marked exacerbation of the condition on the hands, forearms and legs. During the past three months she had lost 9 pounds (4.1 Kg.) in weight. The general history was essentially unimportant, except for gastric distress and symptoms referable to a pathologic condition of the gallbladder and diminution in hearing of twenty years' duration. The patient had considerable pain when the feet were in the dependent position.

She presented generalized bilateral and symmetrical, wrinkled, well defined, erythematous plaques on the arms up to and including the scapular area. Similar plaques were present over the anterior surfaces of the legs from the ankles to the knees, with scattered discoid lesions over the thighs. The skin in the affected areas was very thin and atrophic, with a scant amount of subcutaneous fat, a glazed appearance and scattered telangiectases, especially over the hands. Over both tibiae was a scleroderma-like infiltration.

Examination of the blood revealed 4,450,000 erythrocytes, 5,450 leukocytes and hemoglobin 60 per cent. The differential count showed: lymphocytes, 55 per cent; polymorphonuclears, 36 per cent and eosinophils, 8 per cent—that is, moderate leukopenia with relative lymphocytosis. The basal metabolic rate was + 15.

The results of biopsy were as follows: The epidermis showed a thin non-nucleated scale, considerable acanthosis with lengthening of the rete pegs, occasional intracellular and intercellular edema and an intact basal layer. In the upper part of the corium extending up into the papillae was a loose infiltrate of lymphocytes and macrophages grouped especially about the blood vessels. The collagen fibers here were thin, pale and wavy, while elastic fibers were absent. In the deeper part of the corium the collagen fibers were thicker and horizontally placed, while the elastic fibers were broken up into short, curly fragments. The deeper vessels, especially the arteries, showed thickening of the entire wall, and in some the lumen was nearly occluded. There were small nests of lymphocytic infiltration about these vessels. The sweat glands were normal.

DISCUSSION

DR. WILLIAM ALLEN PUSEY: This condition originally was described by Taylor as multiple idiopathic atrophy of the extremities, which is as good a name as the Latin term, and I offer this as a diagnosis.

DR. DAVID LIEBERTHAL: I agree with the diagnosis of epidermolysis bullosa congenita. The interesting feature is the thickening of the calves. This is, undoubtedly, the primary change, which may then be followed by atrophy.

DR. F. E. SENEAR: Last month I showed a patient with this disorder who presented the edematous as well as the atrophic stage. In that case there was no question but that the former was the early stage of acrodermatitis chronica atrophicans. This woman, however, had crusted lesions on the legs due to scratching and then the scleroderma-like condition of the calf was noticed. The question arose whether this was the early infiltrative stage followed by atrophy or whether it also was a result of the scratching. My opinion is that the fibrous condition is due to repeated attacks of dermatitis.

DR. S. W. BECKER: Pautrier first studied cases of this kind intensively, and I saw in his clinic several cases like this one. He considers the involvement of the legs simply a sclerodermatous condition. The striking thing was that Pautrier said that in Paris about three cases had been shown in the last twenty years, but when he went to Strassburg among Germanic people he saw a great many cases. He was inclined to consider the condition associated with thyroid disturbances.

DR. WILLIAM ALLEN PUSEY: I think that this late atrophy of the skin represents a terminal stage of various conditions. The first of these is extreme

senile atrophy of the skin. Frequently also it is the result of chronic inflammation of the skin of the legs, which ends in atrophy of the skin. I have seen it with late syphilis of the legs. Sometimes it follows true diffuse scleroderma.

PHYSICAL ALLERGY. Presented by DR. OLIVER S. ORMSBY.

A man, aged 35, was first seen in September, 1926; at that time the duration of the disorder was three weeks. From that date until the time of this presentation an eruption had developed following violent physical exercise or the taking of steam baths. The eruption consisted of erythematous macules which appeared within a few minutes after the exciting cause and remained for from several hours to a day or two and then disappeared.

The macules had the configuration of gyrate lesions of multiform erythema. There were no subjective symptoms.

DISCUSSION

DR. JAMES H. MITCHELL: About four years ago I presented a boy who, two or three years previously, during the football season, had had an eruption due to exertion. It was not associated with heat. I asked him to run up and down stairs in the building, which he did. Within a few minutes he returned with a marked urticarial eruption. I asked Dr. Ormsby's patient whether in cold weather he had an eruption if he exerted himself, and he said he did not. The condition must, therefore, be due to heat. In the case I presented it was definitely due to exertion. I have seen two young women in whom a similar condition developed from riding horseback or dancing. Evidently the cases are closely related, but there seems to be some difference as regards heat.

DR. OLIVER S. ORMSBY: I showed this patient in order to emphasize my position relative to allergy. I think that physicians who work with diseases of the skin, which in numerous instances are due to sensitization, should keep the allergic conditions in mind. I think that physical allergy is an appropriate title for this group of conditions, whether they are due to heat, cold, exertion or other physical agents. The interesting feature of this case is that the condition simulates closely a toxic erythema, but I think that no toxic element is present.

OCULOGLANDULAR TULAREMIA. Presented by DR. EDWARD A. OLIVER.

A Negro, aged 17, who was a butcher's assistant and dressed rabbits, first noted redness of the left eye in December, 1931. Within three or four days the glands at the left angle of the jaw began to enlarge. This process progressed for from five to six weeks, after which time the glands were incised. He also had weakness, fever and constitutional symptoms during this time.

Agglutination tests made at the State Laboratory showed a reaction of 1:320 for tularemia.

Examination revealed discrete glands the size of a large nut beneath the left angle of the jaw and smaller ones on the right side. There were two healed incisions on the left side. The glands had decreased two-thirds in size under filtered roentgenotherapy.

A brother was said to have experienced a similar illness.

A CASE FOR DIAGNOSIS (SARCOID? LEPROSY?). Presented by DR. MAX S. WIEN and DR. THEODORE CORNBLEET.

S. G., a Filipino, aged 20, was shown for the first time at the January, 1930, meeting of this society by Dr. Finnerud (ARCH. DERMAT. & SYPH. **22**:339, 1930). The patient was subsequently shown at a meeting of the society in the spring of 1931, at which time a diagnosis of leprosy was suggested, and histologic sections revealing acid-fast bacilli were presented. He was in the Cook County Hospital during a second admission from April 15, 1931, to Aug. 16, 1931, and entered the Carville Leprosarium on Aug. 17, 1931, being discharged on Oct. 23, 1931.

The patient stated that while at Carville he received an exhaustive examination and injections of chaulmoogra oil for three weeks, after which he was discharged.

At the time of presentation the patient showed an entirely different picture than that noted on his previous two admissions to the Cook County Hospital, and no active lesions were present. Here and there over the face and trunk were dispersed coin-sized residual patches of preexisting lesions. The skin had been in this condition since the patient's discharge from Carville in 1931.

Examination revealed a superficial type of patchy atrophy involving the cheeks in a somewhat butterfly arrangement with extension to and involvement of the ears, some areas revealing a pink erythematous flush. The atrophy in general was of a wrinkled type. The neck, trunk and extremities, with the greatest distribution over the extensor surfaces of the arms, back, buttocks and knees, presented numerous discrete discoid areas ranging from the size of a bean to that of a large coin, many of which revealed peripheral bandlike elevations from 3 to 5 mm. in diameter, with central wrinkled atrophy. This varied in intensity in the patches, and in some areas there was nothing more than nummular depigmentation. There was a tendency toward confluence, especially over the elbows and knees, where large mottled patches were noted, with definite wrinkling of the atrophic skin. Confluence was also present over the anterior aspects of the thighs, knees and right buttock. Cutaneous sensation was apparently normal throughout all areas. Serologic examination of the blood gave negative results, as on previous occasions. General physical examination showed no gross pathologic conditions, except for a few carious teeth.

DISCUSSION

DR. S. W. BECKER: I wish to recall the Filipino whom I presented at the same time that this patient was first seen at one of the meetings of the society. My patient had a plaque over the face which showed a tuberculid structure, but in which no acid-fast bacilli could be found. Some time later there was published from the Municipal Sanitarium a report of a case which was almost similar. I discussed this case with Dr. Denney at Carville, to whom the roentgenograms of the bones had been sent; he thought that these patients did not have leprosy but had tuberculosis.

DR. RUBEN NOMLAND: The patient to whom Dr. Becker refers was treated with gold sodium thiosulphate for lupus erythematodes (Leloir); he improved and went back to the Philippines. When the youth who was shown today was first presented by Dr. Oliver and Dr. Finnerud, he was thought to have sarcoid. We examined numerous sections without demonstrating acid-fast bacilli. Dr. Michelson then made the statement that if the condition was leprosy the acid-fast bacillus would be found. However, he was unable to isolate this organism in sections. Subsequently the patient returned with an acute eruption of relatively few weeks' duration. He had dusky red elevations in the places where he now shows the lesions that are sunken in the center. One of the lesions was removed without an anesthetic, and numerous acid-fast bacilli were found in the section. I showed these to a physician from the United States Public Health Service in Chicago, and he said that he thought they were Hansen's bacilli.

DR. H. E. MICHELSON: I thought that the patient had leprosy, but when the bacilli were not found I was not sure. Klingmüller in his book describes a nodular type of leprosy in which the bacilli are not found.

DR. WILLIAM ALLEN PUSEY: In Havana recently I was shown some cases of nodular leprosy of the face that were as nearly as possible replicas of cases shown at Copenhagen as instances of sarcoid. I have no doubt that the diagnoses were correct in both instances. Both leprosy and tuberculosis might produce these closely similar pictures.

DR. MAX S. WIEN: We presented our patient in order to show the change in his clinical appearance. We have not had time to make histologic studies of the lesions as they now exist, but will present a report later.

NOTE.—Histologic examination of three biopsy specimens taken from (1) an infiltrated plaque in the lumbar region, (2) an older lesion on the right arm and (3) a far advanced atrophic lesion on the right buttock showed the following changes: The epidermis was normal. The corium was edematous and contained many sharply defined mantles of infiltration about the blood vessels, sweat glands and nerve fibers, consisting of epithelioid cells and lymphocytes and occasional hollow clear cells. The nerve fibers were greatly thickened, and they as well as the sweat glands were often invaded by cellular infiltrate. The atrophic lesion showed almost complete absence of elastic fibers and a sparsity of collagen fibers in the upper part of the corium. Acid-fast rod-shaped bacilli were present in all specimens, being most numerous in the one taken from the arm. The bacilli were found principally within the nerve fibers, but a few were in the infiltrating cells.

Dr. O. E. Denney, in a letter under date of June 3, 1932, concerning this patient, wrote: "Please be advised that during his stay in Carville, we were unable to confirm the diagnosis of leprosy and the Staff was not unanimous in expression of opinion concerning the clinical picture. During the patient's stay in the hospital, we were unable to find any acid-fast bacilli. The Kolmer, Wassermann and Kahn tests were negative. Blood chemistry was without instructive findings. Pleural fluid which was aspirated was negative for acid-fast bacilli, both in culture and in guinea-pig inoculation."

SCHAMBERG'S DISEASE. Presented by DR. S. W. BECKER.

In a man, aged 53, during the past six months yellowish-brown lesions had developed on the legs. Over both knees and extending downward were ochre yellow plaques, 5 by 15 cm.; a similar plaque was observed on the lateral surface of the right leg. Throughout the lesions were "Cayenne pepper" spots. Over both elbows lichenified, pruritic plaques the color of normal skin were observed.

The Kolmer and Kahn tests of the blood were negative. The urine showed occasional hyaline casts. Examination of the blood revealed 4,500,00 erythrocytes, 10,800 leukocytes and 85 per cent hemoglobin. The differential count showed: polymorphonuclears, 50 per cent; large lymphocytes, 14 per cent; small lymphocytes, 20 per cent; mononuclears, 10 per cent; eosinophils, 4 per cent, and basophils, 2 per cent. The platelets appeared normal. The bleeding time was two minutes, as was the coagulation time. The blood cholesterol was 109 mg. and 104 mg. per hundred cubic centimeters on two occasions. The blood sugar content during fasting was 70 mg. per hundred cubic centimeters at the first determination; after one-half hour it was 102 mg., after two hours, 76 mg. and after three hours, 51 mg., showing an increased sugar tolerance.

DISCUSSION

DR. S. W. BECKER: The first work that was done on Schamberg's disease, with the exception of the clinical and histologic study, was by Dr. Schamberg himself, who reported hypercholesteremia in two cases. I had a patient who had hemochromatosis with high blood cholesterol; he died, presumably from diabetes. Since that time I have examined three patients with Schamberg's disease, but the blood cholesterol has been low and the sugar tolerance has shown an increase rather than a decrease. Whether this is a manifestation of the disease or something incidental, I do not know.

DR. MICHAEL H. EBERT: I have been very much interested in Schamberg's disease, in that in some cases there seems to be a relation between these pigmentary deposits at points of pressure and gastric disturbances. I remember one man who had a peptic ulcer which cleared up with treatment. Following this the pigmentation became absorbed. He also was given some local roentgenotherapy. Since then I have seen several cases with a history of duodenal or peptic ulcer in con-

nection with Schamberg's disease. This suggests some relationship between the gastro-intestinal disturbance and the increased permeability of the capillaries of the skin.

BLASTOMYCOSIS. Presented by DR. F. E. SENEAR and DR. H. RATTNER.

J. H., a Negro, aged 34, a foundry worker, from the department of dermatology, University of Illinois, presented a large patch of dermatitis covering the back of his neck and extending downward to the inferior border of the left scapula. The nape of the neck was the site of a raised, pink, smooth, glistening keloidal scar, which was surrounded by an active border ½ inch (1.27 cm.) wide. The border is purplish and verrucous, sloped abruptly, discharged in some areas and when first seen ten days ago contained scattered tiny epidermal abscesses. The lower half of the patch was most active. Below the large patch there were two discrete coin-sized lesions similar in character. On the left side of the neck a healed pigmented scar was observed.

Organisms were demonstrated by direct smear and in sections. The patient has had no treatment other than remedies that he had bought in drug stores.

The results of biopsy were as follows: The epidermis was acanthotic, in the form of many large papillary projections, and markedly edematous; it contained many small abscesses filled with polymorphonuclears and lymphocytes. There was a thick crustaceous scale lying between these folds. The corium was edematous, had dilated blood vessels, and was filled by a diffuse infiltrate of polymorphonuclears, lymphocytes, plasma cells, mast cells, macrophages and eosinophils, and in places many giant cells. Within some of the giant cells were round, clear, doubly refractile yeast cells.

LUPUS VULGARIS. Presented by DR. JAMES H. MITCHELL and DR. RUBEN NOMLAND.

A woman, aged 64, was first seen at the Central Free Dispensary on Jan. 30, 1932. She gave a history of tuberculous glands in the neck during childhood, the scars of which were pronounced. Beneath the chin was an area of lupus vulgaris somewhat larger than a dollar, with lupomas throughout. A lantern slide in colors and a black and white picture were made on the occasion of the first visit. The treatment consisted of local exposure to ultraviolet rays from a water-cooled quartz mercury vapor arc lamp, general exposure to the air-cooled lamp, the Gerson salt-free diet and the ingestion of large doses of phosphorized cod liver oil. The patient was presented in order to show the remarkable therapeutic effect attained.

DISCUSSION

DR. OLIVER S. ORMSBY: Did the presenters have much trouble in inducing the patient to carry out the treatment?

DR. JAMES H. MITCHELL: The patient is intelligently cooperative, and as far as I can determine has adhered to the diet closely. I received in the mail recently a German preparation designed solely for use in the Gerson diet. It is salt that is free from chloride but has the same taste as the ordinary variety and is said to be entirely innocuous when used in treatment.

SYRINGOCYSTOMA. Presented by DR. L. F. WEBER.

M. M., a pregnant Negress, aged 23, presented a papulofollicular eruption which had been present since childhood. About two years ago it began to extend from the abdomen to the chest. There was no subjective symptom.

The results of biopsy were as follows: The epidermis was normal. In the upper part of the corium several round and ovoid cysts were seen, lined by several layers of epithelial cells and filled with a pale homogeneous mass. There were also several solid longitudinal strands of similar cells. Deeper in the corium were sweat glands which were apparently normal.

DISCUSSION

DR. F. E. SENEAR: This case is interesting for two reasons. The first is the age at which the condition started, if one can depend on the history being correct. I do not recall having seen a case that started at such an early age as 2 years. The second is the fact that the patient has had an eruption on the abdomen for many years, and that only within recent years has it begun to extend to the usual location on the upper portion of the trunk.

DR. CLARK W. FINNERUD: I am sure from the sections the condition is syringocystoma.

DR. ARTHUR W. STILLIANS: Dr. Weidman a few years ago reported a case of tricho-epithelioma on the face and syringocystoma on the chest. He also found three different origins of growth in the same tumor: from the duct, from the skin and from the hair follicles.

CLEVELAND DERMATOLOGICAL SOCIETY

J. R. DRIVER, M.D., *Reporter*

Regular Meeting, May 26, 1932

E. W. NETHERTON, M.D., *Presiding*

CARCINOMATOSIS. Presented by DR. H. F. DE WOLF.

E. B., a white woman, aged 54, from the medical service at the Cleveland City Hospital, was admitted May 18, 1932, complaining of shortness of breath, cough, hemoptysis, loss of weight, pains in the shoulders and arms and lumps over the body. About two years prior to admission, a growth had developed on the right frontotemporal region of the scalp. One year later, the lesion was excised; it was considered to be a sebaceous cyst. Shortly after this operation, more lesions began to appear over the scalp and later over the neck and trunk. These tumors have slowly increased in size. The patient has lost about 50 pounds (22 Kg.) in the year before admission. Six months before admission coughing with some hemoptysis began.

The patient's skin had a yellowish color. Over the scalp there were several dull red nodular lesions, somewhat lobulated, firm, movable and not tender. Widely distributed over the rest of the body, with the exception of the lower extremities, were twelve or fifteen subcutaneous masses of various sizes. The largest of these tumors was in the epigastric region; it was the size of an orange. There was marked enlargement of the axillary lymph glands. Wassermann and Kline tests of the blood were negative. The blood count revealed: red cells, 4,000,000; white cells, 16,500, and hemoglobin, 75 per cent. Examination of the urine gave negative results. Roentgenograms showed metastases to the skull and the lungs. Biopsy had not been done.

DISCUSSION

DR. H. N. COLE: Unfortunately, there has been no opportunity thus far for a specimen to be removed for histologic examination. In regard to the tumor on the scalp, I have seen two or three cases of lymphosarcoma that apparently started in this way. Extensive metastases, such as are seen in this patient, would rule out cylindroma. I am inclined to think that the condition is carcinomatosis. A specimen will be obtained for histologic examination and a report made later.

DR. R. E. BARNEY: It is extremely interesting to see a patient with such an extensive growth in so good a physical condition. The woman is just peppered with malignant growths, yet apparently is otherwise in good health.

DR. J. R. DRIVER: I think that the case is one of lymphosarcoma. This could explain the apparently good general condition of a patient with such widespread metastases. I think that if the condition were carcinoma, the lesions on the scalp would have broken down by this time. The lesions on the abdomen are rather bluish, but I think that this is due to the veins showing through the skin. I do not think that the condition is a melanotic process. I believe that if it proves to be lymphosarcoma, roentgen therapy will give temporary improvement.

DR. L. J. CARSON: I was reading the transactions of the Chicago Dermatological Society, in which Dr. Ormsby discussed a case somewhat similar to this. He thought of the possibilty of an endothelioma, but after all the discussions, there had not been much progress made concerning the clinical results.

DR. H. J. PARKHURST: The clinical appearance of the scalp suggested endothelioma. I have a case in which a diagnosis of endothelioma of the abdomen was made; this tumor also metastasized following complete removal.

LYMPHOGRANULOMA INGUINALE. Presented by DR. H. F. DE WOLF.

J. B., a white man, aged 45, from the service of Dr. H. N. Cole and Dr. J. R. Driver at the Cleveland City Hospital, was admitted on May 25, 1932, complaining of a lump in the right groin. He gave a history of two extramarital exposures, one in January, 1932, and the other about April 20, 1932. Both exposures had been with the same woman. Three or four days after the last exposure a urethral discharge developed. This was followed in a few days by a swelling in the groin which continued to increase slowly in size. With the onset of the swelling in the groin, he began to have fever, chills, severe night sweats and weakness and, in the last three or four weeks, he had lost about 15 pounds (6 Kg.). Systemic symptoms had gradually subsided so that at the time of presentation he had no definite complaints aside from the large, tender mass in the right groin; urethritis was transient, and there was no discharge. The past history did not reveal any venereal disease. The patient is married and has seven children. His wife is in good health.

Examination gave essentially negative results, except for a large, only slightly tender firm mass in the right groin. The mass was the size of a lemon, and the long diameter was over the inguinal ligament. The skin over this mass was dark red and was apparently attached to the underlying structures. The Frei intradermal test was positive.

DISCUSSION

DR. H. F. DE WOLF: I think that this is a typical case of lymphogranuloma inguinale. There is a history of exposure and urethral discharge followed shortly by the onset of adenitis. The urethritis was transient and passed away without treatment. This disease is becoming quite prevalent in Cleveland. Within the last three days, three white men, with this condition have been admitted to the hospital.

DR. E. W. NETHERTON: The patient told me that he had had a primary lesion on the prepuce, a small sore, lasting a few days. How many days is it before the primary sore disappears?

DR. H. F. DE WOLF: As a rule, the external lesion is very transient, so one rarely has an opportunity to see one; usually the duration is a few days. More persistent lesions have been reported, but we have never seen one.

LATE SECONDARY SYPHILIS. Presented by DR. H. F. DE WOLF.

M. W., a Negress, aged 29, from the service of Dr. H. N. Cole and Dr. J. R. Driver at Cleveland City Hospital, stated that about eight months before presentation several small, painless papules had developed on the bridge of the nose. Similar lesions soon developed over the left scapular region. About a month prior to presentation lesions of similar character appeared under the right

axillary region. There had been no subjective symptoms. The patient noted that some of the lesions healed, but new ones continued to appear. She had not had any known venereal infections. The patient had one child, 5 years old. Since its birth she had one miscarriage at seven months and one stillbirth.

Over the bridge of the nose there were several small, dark red, slightly indurated papules. Over the left scapula there was an extensive group of similar lesions. There was a smaller group of a similar character in the right axillary region.

The Wassermann and Kline tests of the blood were both 4 plus. Examination of the spinal fluid showed: four cells per cubic millimeter; the Pandy reaction, 3 plus; the Wassermann reaction, 4 plus in 1 cc., and the gum mastic curve, 5432100000. A microscopic section from one of the lesions was shown.

DISCUSSION

DR. H. N. COLE: When the patient came to the hospital, she had a very unusual condition. The eruption was not symmetical; it was sharply defined and had a reniform shape; however, when one first examined it, the lesion was found to be made up of shiny papules and would make one think of lichenization, but on close examination, there was considerable infiltration, not of a scaling type, and it had this suggestive contour. Moreover, there was a small group of these lesions over the bridge of the nose, which would be quite unusual for lichenization. The three groups of lesions made one think not of an external condition, but of a condition of the blood stream. We made a diagnosis of late secondary syphiloderm.

FOX-FORDYCE DISEASE. Presented by DR. BENJAMIN LEVINE.

E. L., a white woman, aged 41, married, presented a lichenified, papular, pigmented eruption in both axillae, around the nipples of both breasts and over the pubic region, of one year's duration. There was considerable loss of hair in these areas. The Kline slide precipitation test was negative.

DISCUSSION

DR. H. J. PARKHURST: I agree with the diagnosis of Fox-Fordyce's disease, the involvement of the axillae, nipples and pubic regions being quite typical.

DR. L. J. CARSON: I have a patient, a boy, on whom I have tried every remedy without results. I wonder if any one here has been able to do anything for patients with this disease?

DR. H. G. MISKJIAN: It would be worth while to perform a biopsy in this case. The relation of Fox-Fordyce's disease to what is usually termed neurodermite has been under discussion for a long time. The cases of Fox-Fordyce's disease that I have had occasion to study were characterized by a histologic picture which would enable one to differentiate it from a neurodermite. I am not sure that the case presented today is one of true Fox-Fordyce's disease. In spite of the characteristic location of the lesions in the axillae and on the pubic region, certain details, such as the exaggeration of the normal lines of the skin and the numerous quadrangular areas that the intersections of these lines form, make me think that this may well be a case of secondary lichenization or neurodermite. Cases of this type may have given rise to the idea that Fox-Fordyce's disease is only a clinical variety of neurodermite. A biopsy, if it enables us to tell under which heading Dr. Levine's case should be classified, will help us to reach a clearer notion of the nature of Fox-Fordyce's disease.

DR. E. W. NETHERTON: I had occasion to look up material on Fox-Fordyce's disease, and one of the points that Dr. Miskjian has brought up I found to be the case; while the condition appears to be a neurodermite, it is histologically different than neurodermite, which is characterized by folliculitis pierced by a hair in the center of each lesion. I think that in this case the lesions are regular

in contour and definitely symmetrical and show a picture identical to that of Fox-Fordyce's disease. Also, the sparseness of the hair is characteristic. No treatment is known to be of any value.

DR. SIDNEY LITTMAN: I favor the diagnosis of Fox-Fordyce's disease.

DR. BENJAMIN LEVINE: The patient was seen only once before being presented. I shall endeavor to perform a biopsy.

LUPUS ERYTHEMATOSUS (?) Presented by DR. H. F. DE WOLF.

W. S., a white man, aged 35, from the service of Dr. H. N. Cole and Dr. J. R. Driver at Cleveland City Hospital, who had been shown at the meeting of the Cleveland Dermatological Society in February, 1932, complained of the same lesion of the lower lip. The majority of the discussers favored a diagnosis of lupus erythematosus. The lesion had been present for about a year. The patient had been under observation and treatment in the outpatient department of the hospital since Jan. 8, 1932, and had received three injections of gold and sodium thiosulphate, and on one occasion carbon dioxide snow was employed. The lesion was lightly treated by electrodesiccation once. No improvement has occurred.

The lesion is confined to the lower lip. It is a dry, whitish lesion occupying the central two thirds of the vermilion border. A biopsy performed on March 2, 1932, showed stratified squamous epithelium with hyperkeratinization and supported on a small amount of corium. The corium showed a layer of small round cells directly under the epidermis. There was an occasional sebaceous gland. The Wassermann and Kline tests of the blood were negative.

DISCUSSION

DR. J. R. DRIVER: The process looked as if improvement had occurred, though the patient says improvement is just temporary and that the condition becomes worse in a few days. After looking at the section I should be in favor of a diagnosis of lichen planus.

DR. CLAUDE B. NORRIS: I think that together the history and appearance would certainly bear out Dr. Driver's opinion quite well.

DR. H. J. PARKHURST: With the amount of involvement of the lip, I should expect to find more lichen planus inside the cheeks, which I did not find. The appearance of a patch over the zygoma is rather suggestive of early lupus erythematosus. I could see no indications of lichen planus elsewhere.

DR. M. J. GIBANS: I agree with Dr. Parkhurst. The patch on the cheek, about the size of a nickel, looks like early lupus erythematosus.

DR. H. F. DEWOLF: We presented this patient again because treatment for lupus erythematosus was ineffective. We used both gold and sodium thiosulphate and carbon dioxide snow, and recently we tried to destroy the superficial lesions with electrodesiccation. I am not sure that the lesion on the cheek bears any particular relation to the lesion on the lip. I should like to have suggestions as to further treatment. Another factor which I think was suggested before is smoking, and while we advised the patient to stop, he admitted that he smokes cigarets.

DR. H. N. COLE: I think that the condition is lupus erythematosus so far as the section is concerned. I do not think that one can arrive at a fair conclusion from the slide shown, as it was such a poor one. We will get another section. So far as treatment of lupus erythematosus of the lip is concerned, I have seen quite a few patients with this condition, and I think that it is one of the most resistant types with which we have to deal. It is almost impossible to cure it.

DR. R. E. BARNEY: Lichen planus of the lip is also very resistant to treatment. I have a patient now with generalized lichen planus; all of the lesions have

responded to treatment excepting the one on the lip, which still persists, and it is almost like the one shown.

DR. E. W. NETHERTON: I favor a diagnosis of lichen planus because of the lacelike linear deposit all through the lesion. I thought of the same point that Dr. Barney mentioned, that it could be very resistant to treatment. I wonder what the presenter would think of using fractional roentgen treatment and injections of mercury?

MACULAR ATROPHY. Presented by DR. H. N. COLE and DR. J. R. DRIVER.

Delores S., a white girl, aged 10, complained of an eruption on the upper part of the chest of two months' duration. The history was essentially irrelevant. About two months before presentation, peculiar spots appeared on the right side of the neck, and new ones had continued to develop until there were probably fifty of them. There were no subjective symptoms in connection with these lesions, and the patient has been feeling perfectly well.

Distributed over the upper part of the back and the chest were numerous oval, sharply defined lesions, varying in diameter from 1.5 cm. to a few millimeters. There was no inflammatory reaction to these lesions, no scaling and no exudation. On palpation some of them showed the slightest elevation and were quite soft. Others were slightly depressed, and this depression could be palpated with the pulp of the finger. There was a definite break in the continuity of the tissues. On stretching or puckering these areas one noted a demonstrable lack of elasticity in this portion affected.

The Wassermann, Kline and Hinton tests of the blood were all negative. The urine showed nothing unusual. General physical examination gave entirely negative results. There was no evidence of tuberculosis. Examination of the blood showed: hemoglobin, 85 per cent (Talquist); white cells, 5,550, and red cells, 4,256,000; the differential count showed: polymorphonuclears, 44 per cent; large mononuclears, 18 per cent; small mononuclears, 35 per cent, and transitionals, 3 per cent.

A biopsy section taken from one of the depressed areas, stained with hematoxylin and eosin, with Weigert's elastic tissue stain and with van Gieson's connective tissue stain, showed the following picture: In some areas there was a slight mononuclear, cellular infiltration around the vessels in the uppermost layers of the corium. The vessels were widened, and there was some edema around them. In still other areas in this same portion of the section there seemed to be a homogenization of all the tissues just below the epidermis. The papillae seemed to be flattened. The collagen fibers were not made out well. The epidermis was thinner than normal, and with Weigert's connective tissue stain there was noted a lack of elastic fibers. Moreover, throughout the entire section there was more or less absence of the normal amount of sweat glands. Elastic fibers were not very distinct, and there was some swelling of the collagen fibers.

DISCUSSION

DR. H. G. MISKJIAN: This is an interesting case because of the large number of elements and because of the localization. The lesions are all confined to areas around the neck, and on examination one can see lesions in different stages of development. The early lesions are raised, but on examination one can see the lack of elastic fibers. The skin has lost its elasticity. I do not think that there is any doubt as to the diagnosis.

DR. H. N. COLE: This child has a rare dermatosis. I do not think that I have seen more than six or seven of these cases since I have been in private practice. They are thought to be due to some type of systemic infection, for example, an old tuberculosis. Of course, it is well known that one sometimes sees macular atrophy following syphilis; for example, several years ago there was a patient in the City Hospital clinic who showed a typical example of the con-

dition described by Schweninger-Buzzi. This patient had old tabes, and I am inclined to think that many of the so-called examples of Schweninger-Buzzi disease are examples of syphilitic macular atrophy. In this girl we can find no evidence of syphilis. Most of the cases of macular atrophy that I have seen have been in girls or women, usually over the areas that are involved in this case. I have no explanation as to its cause. Of course, the outlook as to recovery is not favorable. The microscopic preparations show nicely the absence of elastic fibers in the areas affected. We have given the child small doses of corrosive mercuric chloride by mouth, but expect no results from its use.

Book Reviews

Common Skin Diseases. By A. C. Roxburgh, M.D., M.A., B.Ch., Cantab., F.R.C.P. Price, 18 shillings, net. Pp. 310, with 8 plates and 110 illustrations. London: H. K. Lewis & Co., Ltd., 1932.

This is a fine book; we were about to say a fine little book, but, as a matter of fact, it is a book of over 300 pages, and is crammed full of the wisdom of an experienced dermatologist. It is what it purports to be, a treatise on common diseases of the skin. The chief criticism that the reviewer makes is a rare one about textbooks on diseases of the skin; he wishes that the author had made it longer so that he might have covered the whole of cutaneous diseases in the wise and practical way that he has covered the commoner ones. It is a personal book in which the author frankly expresses his personal judgments and his personal experiences. If one had room to quote, one could quote innumerable sentences illustrating this. It is a book that can particularly be recommended to the general practitioner. It has tables of differential diagnosis, so that the rare diseases that are not considered in the text can be found and studied in larger texts, and therefore it does not fail the practitioner here; it is particularly useful to him in the treatment of diseases of the skin. Roxburgh's comments on treatment are those of an experienced able clinician who knows the tried methods that he recommends, and who is so firmly anchored in experience that he is not carried away by new methods that have not yet had sufficient trial, or that under sufficient trial have actually shown no advantage over older ones. The work is especially to be commended for its handling of the subject of treatment. The author writes excellent English; his style is simple, informal, even conversational, and plain, so that the book is easy to read. Both in form and in substance it deserves success.

Directory of Dermatologic Societies *

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

J. Frederick Burgess, President, Drummond Medical Bldg., Montreal.
B. Usher, Secretary-Treasurer, Medical Arts Bldg., Sherbrooke St., W., Montreal.

Royal Society of Medicine, Section of Dermatology

A. M. H. Gray, President, 30 New Cavendish St., W. 1, London.
W. N. Goldsmith, Secretary, 6, Upper Wimpole St., W. 1, London.

NATIONAL DERMATOLOGIC SOCIETIES

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

Francis Eugene Senear, Chairman, 55 E. Washington St., Chicago.
Harry R. Foerster, Secretary, 208 E. Wisconsin Ave., Milwaukee.
Place: Milwaukee. Time: June 12-16, 1933.

American Dermatological Association

Fred Wise, President, 200 W. 59th St., New York.
W. H. Guy, Secretary, 500 Penn Ave., Pittsburgh.
Place: Chicago. Time: 1933.

SECTIONAL DERMATOLOGIC SOCIETIES

Baltimore-Washington Dermatological Society

Harry M. Robinson, President, 106 E. Chase St., Baltimore.
M. H. Goodman, Secretary, 401 Medical Arts Bldg., Baltimore.

Central States Dermatological Association

Emmett C. Troxell, President, 74 W. Adams St., Detroit.
William G. Saunders, Secretary, 9203 Grand River Ave., Detroit.

Iowa and Western Illinois Dermatological Association

J. C. Kessler, President, University Hospital, Iowa City, Iowa.
Robert E. Jameson, Secretary, 201 West Second St., Davenport, Iowa.

New England Dermatological Society

Arthur M. Greenwood, President, 416 Marlboro St., Boston.
William P. Boardman, Secretary, 388 Marlboro St., Boston.

Southern Medical Association, Section on Dermatology and Syphilology

Andrew L. Glaze, Chairman, 1928 First Avenue, Birmingham, Ala.
Dudley C. Smith, Secretary, University, Va.
Place: Richmond, Va. Time: November, 1933.

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* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

STATE DERMATOLOGIC SOCIETIES

Florida Society of Dermatology and Syphilology

Chairman for each meeting is elected from city in which meeting is held.
Frank Wilson, Secretary, 310 Greenleaf & Crosby Bldg., Jacksonville, Fla.
Place: Jacksonville, Tampa, Miami and place of meeting of state medical society.
Time: Quarterly.

Louisiana Dermatological Society

J. A. Devron, President, 150 Baronne St., New Orleans.
M. T. Van Studdiford, Secretary-Treasurer, 912 Pere Marquette Bldg., New Orleans.

Medical Society of the State of New York, Section on Dermatology and Syphilology

Paul E. Bechet, Chairman, 55 Park Ave., New York.
Herbert H. Baukus, Secretary, 925 Delaware Ave., Buffalo.

Medical Society of the State of Pennsylvania Section on Dermatology

Stanley Crawford, President, 200, 9th St., Pittsburgh.
Robert L. Gilman, Secretary, 1930 Chestnut St., Philadelphia.

Michigan State Medical Society, Section on Dermatology and Syphilology

Cyril K. Valade, Chairman, 1604 Eaton Tower, Detroit.
George H. Belote, Secretary, University Hospital, Ann Arbor.

Minnesota Dermatological Society

H. N. Klein, President, 350 St. Peter St., St. Paul.
D. D. Turnacliff, Secretary, 407 Medical Arts Bldg., Minneapolis.

Oklahoma Dermatological Association

William E. Eastland, President, 117 N. Broadway, Oklahoma City.
C. L. Brundage, Secretary, 616 Medical Arts Bldg., Oklahoma City.

Texas Dermatological Society

T. J. Calhoun, President, 1719 Pacific Ave., Dallas.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.

LOCAL DERMATOLOGIC SOCIETIES

Atlanta Dermatological Society

Francis G. Jones, President, 384 Peachtree St., Atlanta, Ga.
Charles A. Wilkins, Secretary, Medical Arts Bldg., Atlanta, Ga.

Bronx Dermatological Society

Adolph Rostenberg, Chairman, 152 E. 179th St., New York.
Theodore Rosenthal, Secretary-Treasurer, 115 W. 86th St., New York.

Brooklyn Dermatological Society

Louis J. Frank, President, 1367 Eastern Parkway, Brooklyn.
George F. Price, Secretary, 884 Lincoln Place, Brooklyn.
Time: Third Monday of each month except June, July, August and September.

Buffalo Dermatological Society

Herbert H. Bauckus, Presidennt, 925 Delaware Ave., Buffalo.
William F. Hoover, Secretary, 333 Linwood Ave., Buffalo.

Chicago Dermatological Society

Michael Ebert, President, 25 E. Washington St., Chicago.
E. A. Oliver, Secretary, 55 E. Washington St., Chicago.

Cincinnati Dermatological Society

Ralph R. DuCasse, President, Carew Tower, Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.

Cleveland Dermatological Society

E. W. Netherton, President, Cleveland Clinic, Euclid Ave. and E. 93d St., Cleveland.
H. G. Miskjian, Secretary, Rose Bldg., Cleveland.

Detroit Dermatological Society

Emmett C. Troxell, President, 74 W. Adams Ave., Detroit.
William G. Saunders, Secretary-Treasurer, 9203 Grand River Ave., Detroit.

Los Angeles Dermatological Society

Samuel Ayres, Jr., Chairman, 2007 Wilshire Blvd., Los Angeles.
Louis F. X. Wilhelm, Secretary, 1401 South Hope St., Los Angeles.

Manhattan Dermatologic Society

Fred Wise, Chairman, 200 West Fifty-Ninth St., New York.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

Montreal Dermatological Society

J. F. Burgess, President, Drummond Medical Bldg., Montreal, Canada.
B. Usher, Secretary-Treasurer, Medical Arts Bldg., Sherbrooke St., W., Montreal, Canada.

New York Academy of Medicine, Section of Dermatology and Syphilis

A. Benson Cannon, Chairman, 371 Park Ave., New York.
Louis Chargin, Secretary, 1 W. 85th St., New York.

New York Dermatological Society

George M. MacKee, President, 200 W. 59th St., New York.
Edward R. Maloney, Secretary, 853 7th Ave., New York.

Omaha Dermatological Society

H. C. Sumney, Chairman, 1011 W. O. W. Bldg., Omaha.
Donald J. Wilson, Secretary, 1216 Medical Arts Bldg., Omaha.

Philadelphia Dermatological Society

Frederick D. Weidman, Chairman, 1930 Chestnut St., Philadelphia.
Robert L. Gilman, Secretary, 1930 Chestnut St., Philadelphia.

Pittsburgh Dermatological Society

Claude B. Norris, Chairman, 244 Lincoln Ave., Youngstown, Ohio.
Frederick Amshel, Secretary, 3401 5th Ave., Pittsburgh.

St. Louis Dermatological Society

Richard S. Weiss, President, 3720 Washington Blvd., St. Louis.
M. F. Engman, Jr., Secretary-Treasurer, 3720 Washington Blvd., St. Louis.

San Francisco Dermatological Society

Charles Schoff, President, 1127, 11th St., Sacramento, Calif.
John M. Graves, Secretary, 909 Hyde St., San Francisco.